

**PREVALENCE AND RISK FACTORS OF CHRONIC
OBSTRUCTIVE PULMONARY DISEASE IN PAST
PULMONARY TUBERCULOSIS PATIENTS,
KHARTOUM STATE, SUDAN**

Rashid Kamal Khalid Osman

**Supervisor:
Professor Gunnar Bjune**

**Co-supervisor:
Professor Asma El Sony**

**University of Oslo
Faculty of Medicine
Institute of Health and Society
Section for International Health
Collaborating partner Epidemiological Laboratory, Sudan
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DEDICATION

*“To the soul of my dear father, may he rest in peace
To my beloved mother for her care and support
To my brothers and sisters for their help
And to Ahmed”*

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LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
BOLD	Burden of Obstructive Lung Diseases Study
BMI	Body Mass Index
COPD	Chronic Obstructive Pulmonary Disease
DALYs	Disability-Adjusted Life Years
DOTS	Directly Observed Treatment Short-course
EMRO	Eastern Mediterranean Regional Office
Epi-Lab	Epidemiological Laboratory
FMOH	Federal Ministry of Health
FEV1	Forced Expiratory Volume in one second
FVC	Forced Vital Capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HIV	Human Immunodeficiency Virus
IUATLD	International Union against Tuberculosis and Lung Diseases
LHL	Norwegian Heart and Lung Association
LLN	Lower Limit of Normal
MDR TB	Multi-Drug Resistant Tuberculosis
MMPs	Matrix Metalloproteinases
NCDs	Non-Communicable Diseases
NGOs	Non-Governmental Organization
NTP	National Tuberculosis Program
OR	Odds Ratio
PTB	Pulmonary Tuberculosis
PPTB	Past Pulmonary Tuberculosis
SMOH	State Ministry of Health
SPSS	Statistical Package for the Social Sciences software
TB	Tuberculosis
TBMUs	Tuberculosis Management Units
UIO	University of Oslo
WHO	World Health Organization

ABSTRACT

PREVALENCE AND RISK FACTORS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PAST PULMONARY TUBERCULOSIS PATIENTS, KHARTOUM STATE, SUDAN

R K Osman¹, G Bjune², and A El Sony³

¹MD, Epi-Lab, Khartoum, Sudan, MPhil International Community Health, University of Oslo, Norway.

²Professor, Institute of Health and Society, Faculty of Medicine, University of Oslo, Norway.

³Professor, Epi-Lab, Khartoum, Sudan. Past-president of the IUATLD

Background: Chronic Obstructive Pulmonary Disease (COPD) and Pulmonary Tuberculosis (PTB) constitute a significant public health problem, especially in low and middle income countries. Although, smoking is considered to be a significant risk factor for COPD, further research is necessary to identify risk factors other than smoking, especially in low and middle income countries where the greatest impact of COPD is expected to occur. Not only there is an increasing interest for non-tobacco risk factors, but also there is an emerging evidence that past PTB is a significant risk factor for COPD.

Objectives: The study major objective is to measure the prevalence and risk factors of COPD among Past Pulmonary Tuberculosis (PPTB) patients. Furthermore, to identify the effect of smoking and delayed TB treatment in the development of COPD.

Methods: This is a retrospective cross-sectional study conducted among PPTB subjects and their age and sex matched controls. A total of 136 patients with PPTB was selected from the chest referral clinic at Omdurman teaching hospital after meeting the inclusion and exclusion criteria and matched with 136 controls. Data was collected using structured questionnaires during face to face interview. Then the study participants underwent lung function assessment using spirometry. PPTB diagnosis was based on positive sputum smear results, while COPD was defined as a post-bronchodilator FEV1/FVC <0.7

Results: Prevalence of COPD among PPTB subjects (mean age, 43.97 ± 8.51 years) was 8.8%. PPTB was an independent risk factor and the strongest predictor for COPD with an odds ratio of 12.39 after adjusting for confounding by age, gender, occupational exposure, biomass fuel and smoking did not affect the association. Delayed TB treatment was a risk factor for COPD [OR: 4.09 (95% CI 1.17-14.32)].

Conclusion: PPTB and delayed TB treatment are important risk factors for COPD and should be specifically considered if the burden of COPD is to be reduced in low and middle income countries with an associated TB burden.

Keywords: Pulmonary tuberculosis, COPD, airflow obstruction, delayed tuberculosis treatment, spirometry, low and middle income countries

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1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) and Tuberculosis (TB) constitute a significant public health problem, especially in low and middle income countries.

COPD is expected to become the third leading cause of death worldwide by 2020 according to the projection of the global burden of disease study (1).

In 2004, 64 million people were estimated to have COPD worldwide (2). Despite that COPD is often under-diagnosed and under-reported therefore the morbidity and mortality data related to COPD could be underestimated (1).

According to the recent report from the global burden of disease study, in 2010, COPD stepped up as the third compared to the fourth cause of death in 1990, although the deaths had declined by 7 %, falling from 3.1 to 2.9 million deaths (3).

Chronic respiratory diseases all together accounted for 4.7% of global lost disability adjusted life years (DALYs), with COPD making up two-thirds of the total (4). Among the non-communicable diseases (NCDs) at a global level, only COPD and congenital anomalies have declined. The decline is due to the decrease in other determinants of COPD such as indoor air pollution in India and China, in spite of the increase in the cumulative exposure to tobacco (4).

While TB is the second leading cause of death worldwide, second only to HIV among the infectious diseases. More than one million people die from TB each year, 95% of these deaths occur in low and middle income countries (5).

In 2012, TB killed 1.3 million people (5) worldwide compared to 1.5 two decades ago, dropping from the sixth to the tenth rank (3) despite that, TB still remained among the top ten leading causes of death.

HIV/AIDS and TB were the main causes of lost DALYs for young adult men from 15–39 years of age, TB alone accounted for 2.0% of all DALYs lost (4).

Although TB burden has significantly reduced in Sudan since the 1990s, recent estimates suggest that there is nevertheless a substantial TB burden in the country. During 2012, the estimated TB mortality rate was 22 per 100,000 populations, the prevalence rate was 207 per 100,000 populations and incidence rate was 114 per 100,000 populations (5).

Sudan is also considered to be among the high TB/HIV burden countries according to the WHO global tuberculosis report of 2013. HIV positive incident TB cases were estimated to be 4,300 cases and the incident rate was 12 per 100,000 populations (5).

2. LITERATURE REVIEW

COPD is a leading cause of morbidity and mortality worldwide and results in significant and increasing economic and social burden. The chronic airflow limitation distinctive of COPD, is believed to be attributable to a mixture of small airway disease, namely obstructive bronchitis, and parenchymal destruction, namely emphysema, the relative contributions of which vary from person to person (1).

2.1 Definition of COPD

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines chronic obstructive pulmonary disease as, “*COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients*” (1).

2.2 Burden of COPD

COPD is an important cause of death globally. According to the projection of the global burden of disease, COPD is expected to become the third leading cause of death worldwide by 2020 (2). However, another projection, estimated that COPD will become the fourth cause of death by 2030 (6).

The data about COPD morbidity such as emergency visits and hospitalization are limited. The available data indicates that COPD morbidity increases by age and often affected by comorbidity that may impact patients’ health status and interfere with COPD management (1).

The Burden of Obstructive Lung Diseases Study (BOLD) is carrying out surveys in several countries and has documented more severe disease than previously estimated, with a substantial prevalence of COPD among never smokers (7).

In sub-Saharan Africa, the prevalence of COPD ranged between 4.1 to 24.8% (7) due to different methodologies and definitions used to estimate the prevalence of COPD (8). While in the Eastern Mediterranean, the estimates suggest that there are 3.3 million people suffer from COPD in the region (2).

2.2.1 COPD in Sudan

Data on COPD burden in Sudan is very limited. However, recently the Epidemiological Laboratory (Epi-Lab) a local Non-Governmental Organization (NGO), in collaboration with BOLD at the Imperial College of Science, is carrying out a survey in Khartoum state to measure the prevalence of COPD and its risk factors. The results of which, when published, will be the first attempt to study COPD burden in a large scale survey that has been conducted in Khartoum state.

Studies that were conducted on the prevalence of COPD in Sudan, are scarce and involving only certain population. In fact, there are only two studies; one was conducted among chromite miners and the other enrolled coronary artery disease patients.

Earlier, Ballal reported that the prevalence of chronic bronchitis in chromite ore miners was 26%, based on respiratory symptoms and determination of FEV1, FVC and FEV1/FVC% (9).

In a hospital based study conducted in Khartoum State (10), including 59 catheter diagnosed coronary artery disease patients, COPD (defined as FEV1 < 80% of predicted) was prevalent in 11 (28%) subjects.

Reports from the Federal Ministry of Sudan tend to add COPD to other chronic respiratory diseases and barely estimate COPD alone. A look on the burden of respiratory diseases can hence allow us to relatively estimate COPD burden in Sudan.

Chronic respiratory diseases ranked as the tenth among the top ten leading causes of death, in the country, accounting for 3 % of the total deaths in 2011. Chronic respiratory diseases and

asthma killed 687 and 774 people respectively (11). Their toll accounted for 6 % of total deaths, which was equal to the percentage of the first cause of death (malignant neoplasms) and higher than the third (pneumonia). Additionally, most of the deaths were in Khartoum State (11).

Furthermore, chronic respiratory diseases as a group ranked as the fourth among the top ten diseases seen in the outpatient clinics excluding pneumonia which came second to malaria. They account for 19 per 1000 populations in the whole country while for Khartoum state the prevalence of respiratory disease was 34 per 1000 population in 2011(11).

It is of importance to point out that the term COPD is unusual to the public and even to some physicians in many different parts of the world (12). In fact, in some parts of the world, the term asthma is used to describe chronic respiratory diseases altogether.

2.3 Diagnosis of COPD

COPD diagnosis should be considered in any patient who has shortness of breath, chronic cough or phlegm, and history of exposure to the risk factors of the disease. Spirometry is necessary to make the diagnosis in this clinical context; the presence of post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of persistent airflow limitation and hence a diagnosis of COPD (1).

2.3.1 Symptoms

Chronic cough and sputum production may precede the development of airflow limitation by many years. Conversely, a significant airflow limitation may develop without the presence of a chronic productive cough (1).


The major cause of disability and anxiety associated with COPD is due to dyspnea, which is a cardinal symptom of the disease. Typical patients with COPD describe their shortness of breath as a sense of increased effort to breathe, heaviness, air hunger or gasping (13).

Chronic cough is frequently the first symptom to develop in COPD patients. In the beginning, the cough might be intermittent, but later it exists every day and often throughout the day. It is worth mentioning that some patients may develop COPD but without the existence of chronic cough (1).

Patients with COPD usually bring up small quantities of tenacious sputum after coughing. Patients that produce large amount of sputum may have underlying bronchiectasis. The epidemiological definition of chronic bronchitis is regular production of sputum for 3 or more months in two consecutive years (1).

Wheeze and chest tightness are non-specific symptoms that may vary throughout a single day and between days. Absence of these symptoms does not exclude the diagnosis of COPD, nor does their presence confirm the diagnosis of asthma (1).

Figure 1: Key indicators for considering COPD diagnosis



Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD.

- **Dyspnea that is:** Progressive (worsens over time).
Usually worse with exercise.
Persistent (present every day).
Described by the patient as an "increased effort to breathe," "heaviness," "air hunger," or "gasping."
- **Chronic cough:** May be intermittent and may be unproductive.
- **Chronic sputum production:** Any pattern of chronic sputum production may indicate COPD.
- **History of exposure to risk factors:**
Tobacco smoke (including popular local preparations).
Occupational dusts and chemicals.
Smoke from home cooking and heating fuel.

Source: The Global Initiative for Chronic Obstructive Lung Disease (GOLD)

2.3.2 Spirometry

Spirometry is the most reproducible and objective measurement of airflow limitation now available (1). It detects individuals with excessive lung function loss who are at a higher risk of developing disabling lung function impairment or who have the disease already. Spirometric measurements are evaluated by comparison of the results with appropriate reference values based on age, height, gender and race. A post-bronchodilator $FEV_1/FVC < 0.70$ confirms a diagnosis of airflow obstruction (1).

Some suggest using a cutoff based on the lower limit of normal (LLN) values for FEV_1/FVC than the use of the fixed ratio to define airflow obstruction. They claim that, the fixed FEV_1/FVC ratio may result in more frequent diagnosis of COPD in elderly, and less frequent diagnosis in adults younger than 45 years especially with mild disease. However, it is difficult to decide which of these criteria are correct (15).

Nonetheless, LLN values are greatly dependent on the choice of valid reference equations using post-bronchodilator FEV_1 , and there are neither

longitudinal studies validating the use of LLN nor studies using reference equations in population in which the major cause of COPD is not smoking (1).

The severity grades of COPD are shown in table 2, as proposed by GOLD, showing four grades of airflow obstruction, using cutoff points, ranging from mild to very severe obstruction.

Forced Expiratory Volume in One

Second (FEV_1): The volume of air exhaled during the first second of a forced expiratory maneuver, expressed in liter (14). A lower than normal value may indicate an obstructive lung disease.

Forced Vital Capacity (FVC): The maximal amount of air that can be exhaled forcefully after a maximal inspiration, expressed in liter (14). A lower than normal value indicates a restrictive lung disease and it may also be reduced in severe obstructive diseases.

Figure 2: Spirometric classification of COPD severity



<u>Stage</u>	<u>Characteristics</u>
I: Mild COPD	<ul style="list-style-type: none">• $FEV_1/FVC < 70\%$• $FEV_1 \geq 80\%$ predicted
II: Moderate COPD	<ul style="list-style-type: none">• $FEV_1/FVC < 70\%$• $50\% \leq FEV_1 < 80\%$ predicted
III: Severe COPD	<ul style="list-style-type: none">• $FEV_1/FVC < 70\%$• $30\% \leq FEV_1 < 50\%$ predicted
IV: Very Severe COPD	<ul style="list-style-type: none">• $FEV_1/FVC < 70\%$• $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Source: The Global Initiative for Chronic Obstructive Lung Disease (GOLD)

2.4 Risk factors of COPD

Although smoking is considered to be important risk factors for COPD, there is an increasing interest in non-tobacco risk factors. Indoor air pollution from biomass fuel smoke exposure, exposure to occupational dusts and certain gases, past history of pulmonary tuberculosis, chronic asthma, poor socioeconomic status, and genetic factors (e.g. Alpha 1-antitrypsin deficiency) are recognized as potential risk factors (16). Other potential contributing risk factors include outdoor air pollution, allergy and bronchial hyper-responsiveness, prematurity, low birth weight and certain respiratory infections during childhood (17).

2.5 Past pulmonary tuberculosis is associated with COPD

There is a growing evidence that, past pulmonary tuberculosis (PPTB) is a risk factor for the development of COPD (18-21).

In a large population based multicenter study, including 5571 patients conducted in five Latin American cities, Menezes et al (18) found that the overall prevalence of airflow obstruction among those with a history of TB was 30.7 %. History of PTB increased the risk of COPD by

4.1 times for men and 1.7 times for women, even after adjustment for age, sex, education, ethnic origin, exposure to dust and smoke, and respiratory morbidity in childhood.

In another large study, including 8066 subjects from China, Lam et al reported that prior TB remained independently associated with an increased risk of airflow obstruction even after adjustment for exposure to passive smoking, biomass fuel, and dust (19). Furthermore, the study concluded that the relationship between prior TB and airflow obstruction remained significant even after the adjustment for smoking. The overall prevalence of airflow obstruction was 6.5% (95% CI, 5.9-7.0), and it was similar in both men (6.4%) and women (6.5%).

In a different study conducted in Taiwan, including 3,176 PPTB cases and 15,880 control subjects, Lee and his colleagues noted that the TB group had a significantly higher risk of developing COPD than the control group (7.6% vs. 3.9% $p<0.001$). (20)

Apart from the other risk factors such as age, male sex, and low income, history of TB was an independent risk factor for developing COPD and its impact was sustained for at least six years after TB diagnosis.

It was also found that the delay in anti-TB treatment was an independent risk factor (Hazard Ratio 1.005 [1.003–1.007]) and had a dose response relationship with the risk of developing COPD (20).

In his review of population based and occupational studies conducted in South African, Ehrlich et al (21) found that, chronic chest symptoms and lung function loss were consistently associated with history of PTB, whether measured by self-report or prospectively in the cohort studies. For spirometrically defined COPD, the odds ratio range was 2.6–8.9, depending on the definition of COPD according to the different studies reviewed. Combined obstructive/restrictive lung function loss was the most common functional outcome, with a net obstructive effect (21).

2.6 Lung pathology, pulmonary tuberculosis and COPD

Pulmonary tuberculosis (PTB) histopathologic findings include the formation of caseating granuloma, tissue liquefaction, and cavity formation (22). When these occur in the lung, they result in permanent anatomic changes. This results in pulmonary sequelae that are characterized by bronchial and parenchymal structural changes, including bronchovascular distortion, bronchiectasis, emphysematous changes, and fibrotic bands (22).

The pathophysiology of airflow obstruction in tuberculosis is hypothetical and could be multifactorial in nature. Endobronchial involvement may produce localized bronchial obstruction and fibrosis, whereas tuberculous lymphadenopathy can cause extrinsic bronchial compression (23). Parenchymal lung destruction can affect pulmonary compliance resulting in an increased tendency for peripheral airways collapse and subsequent air trapping (23).

Several studies tested the pulmonary function in PTB subjects and demonstrated variable patterns and severity of pulmonary function impairment. These studies showed restrictive, obstructive, or mixed patterns ranging from normal to severe impairment (24-26).

It was also shown that, following the completion of PTB treatment, about two-thirds of patients have pulmonary function abnormalities (20), with obstructive defect being the main abnormality.

As reported from South Africa, the severity of lung damage causing reduced pulmonary impairment is directly associated with the number of PTB episodes among patients suffering from silicosis (26).

Recently identified (27), the key mediator for the matrix destruction and cavitations are the matrix metalloproteinases (MMPs) produced by monocytes and neutrophils in the caseous granulomatous inflammation of the typical tuberculosis histologic findings. The MMPs have also been shown to mediate the pathogenesis of COPD and predict its pulmonary functional decline (28).

As elucidated, it is possible that a combination of the damage in the airways and the lung parenchyma results in ventilatory abnormalities that lead to lung function impairment and the subsequent development of airflow obstruction (19).

2.7 Diagnostic and treatment delay

Delay in diagnosis and treatment of TB combats an effective tuberculosis program. The total delay is vital for both the patients and the control program resulting in severe form of disease and increased mortality rate, and unhalted transmission (29).

Studies conducted on the delay of diagnosis and treatment of TB relied on different definitions. However, they showed that the delay could be attributed to patients and the health care provider or health system delay. Some studies defined diagnostic delay from the onset of the symptoms till the diagnosis is confirmed (diagnostic delay) while others regard delay till the patient start treatment (treatment delay) (29).

The length of total delay was reported across all continents and extremely differed among countries. It was also observed whether investigating low or high endemic countries, the total diagnostic delay ranged within 60–90 days (29).

Some studies reported that, the total TB delay was mostly attributed to the patient delay (time interval between the appearance of symptoms until the first visit to a medical facility) for instance in Nigeria (30) and South Africa (31). Conversely, some studies found that the total delay was mostly attributed to health system delay (time interval from the first consultation until the date of TB diagnosis) for example in Ethiopia (32).

Factors associated with the total delay are influenced by either or both the patient and health system delay. Factors related to patient delay were alcohol or substance abuse, poverty, low access to health care facilities, rural residence, old age, belonging to an indigenous group and incomprehensive attitudes, beliefs and knowledge about TB (29). While factors linked to health care delay were the coexistence of chronic cough and/or other lung diseases, having extra-pulmonary or negative sputum smear TB, absence of haemoptysis or less severe and

indifferent symptoms, weak health care infrastructure and seeking traditional and private practitioners first (29).

In Sudan, diagnostic delay varied according to urban or rural setting, the median total pre-treatment delay was 53 days and 64.5 days in Khartoum state (33) and Gezira state (34), respectively.

In addition to increasing the severity of TB and further transmission, diagnosis and treatment delay may have long-term pulmonary sequelae and render the development of COPD (20). Delay in anti-TB treatment was an independent risk factor (Hazard Ratio 1.005 [1.003–1.007]) for the development of COPD. Furthermore, a longer delay in anti-TB treatment was significantly associated with the development of COPD (20).

2.8 Sudan's profile

Sudan was the largest country in Africa till the separation of South Sudan in 2011. Sudan has 18 states, with an estimated area of 1,886,068 km² (35) and a population of approximately 37 million (36). The population reveals a cultural and ethnic diversity with several hundred tribal groups speaking over 134 languages (37).

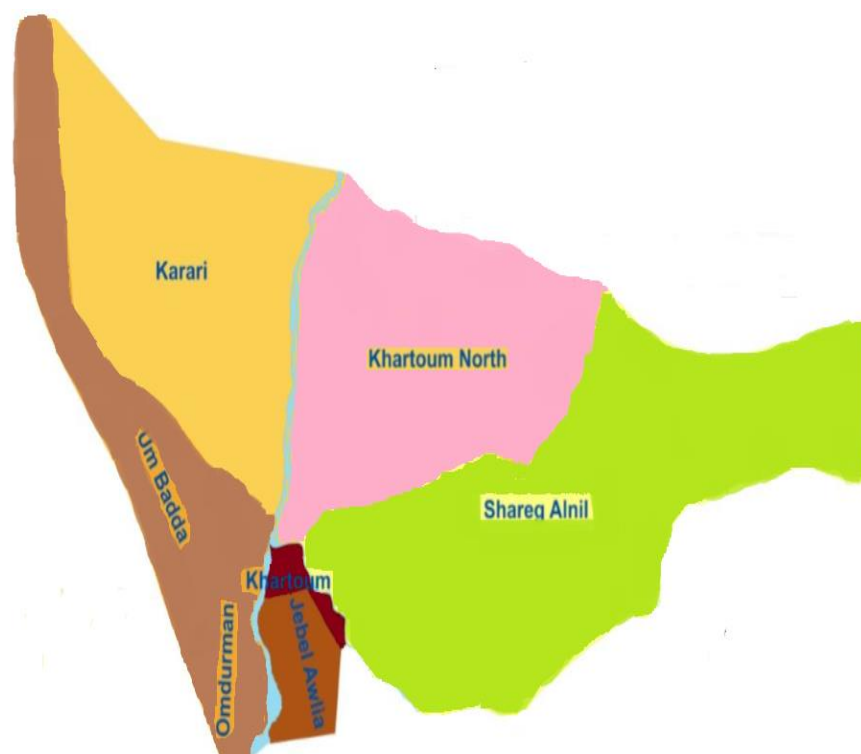
2.8.1 Sudan's health profile

In 2011, the under-five mortality rate was 86 per 1000 live births and life expectancy at birth was 62 years for both sexes. The total expenditure on health per capita was 180 (Intl \$) falling far below the regional average (38).

Figure 3: Sudan boundaries and administrative regions, states



Figure 4: Khartoum state localities



2.8.2 Sudan's health system

The health system in Sudan is organized in three layers comprising of, the Federal Ministry of Health (FMOH), the State Ministry of Health (SMOH) and the Local Health System (39).

Primary health care is delivered through basic health units, for which the health center serves as referral point. It is notable mentioning that vertical programs, particularly TB and the Expanded Programme on Immunization work through these primary level facilities, but also sometimes establish independent posts in peripheral areas (39).

Health centers are managed by the localities while the rural hospitals, which have a capacity of 50 to 100 beds, are managed by the SMOH. Tertiary hospitals, including teaching, specialized, and general hospitals, are located in state capitals and are operated by the State governments (39). In addition, the FMOH operates 17 tertiary-level hospitals. However, the lowest level facilities, even though they outnumber the highest, are declining in recent years and some are not functioning, moreover there are significant disparities in the geographic distribution of health facilities (39). In addition to FMOH and SMOH, the health services are provided through different partners such as, Armed Forces, Police, Ministry of Higher Education, private sector and NGOs (40).

2.8.3 Sudan National Tuberculosis Program

The National Tuberculosis Programme (NTP) was established in 1974, but prior to 1990, the NTP was poorly implemented and hospital based (41). In 1993, regular monitoring for case finding and treatment was initiated, with the adoption of the WHO's policy package for tuberculosis control strategy Directly-Observed Treatment Short-course (DOTS). Since 1995, the NTP has been receiving technical assistance from the Norwegian Heart and Lung Association (LHL), the International Union against Tuberculosis and Lung Diseases (IUATLD) and the WHO (42). TB services are provided by the NTP, the private sector and also by NGOs who provide care mainly for displaced people (43). Although Sudan NTP announced 100% DOTS coverage since 2003, case detection rates remained invariable,

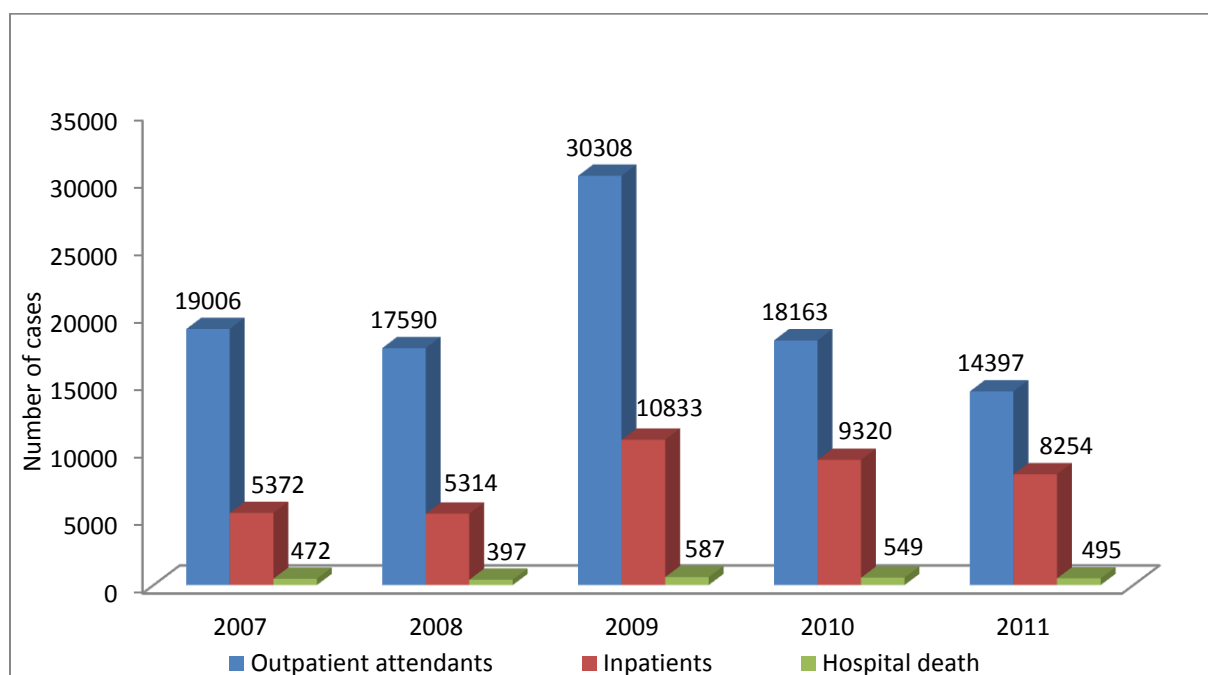
however with decentralization of TB services (44), the success rates raised dramatically reaching 81% by the year 2010 (11). Nevertheless, NTP is facing several constraints in implementing DOTS strategy efficiently, such as long standing civil war, under-reporting and recording, unavailability of HIV testing in some centers, high default rates, and the emergence of Multi-Drug Resistant Tuberculosis (MDR TB).

2.8.4 Burden of TB in Sudan

Recent estimates from the WHO suggested that Sudan has a substantial TB burden. In 2012, the estimated TB mortality rate was 22 per 100,000 populations, while the prevalence rate was 207 per 100,000 populations and incidence rate was 114 per 100,000 populations (5).

The estimated annual risk of infection is 1.2 , which means that among 100,000 populations there is an estimated 120 new TB cases annually of whom 50% are new smear positive cases (11). As shown in figure 5, the total number of TB cases (outpatients, inpatients and hospital deaths) nearly remained static except for the year 2009 in which the number increased dramatically. In 2011, the highest notified cases were in Khartoum state accounting for 5537 cases while 388 patients died in hospitals (11).

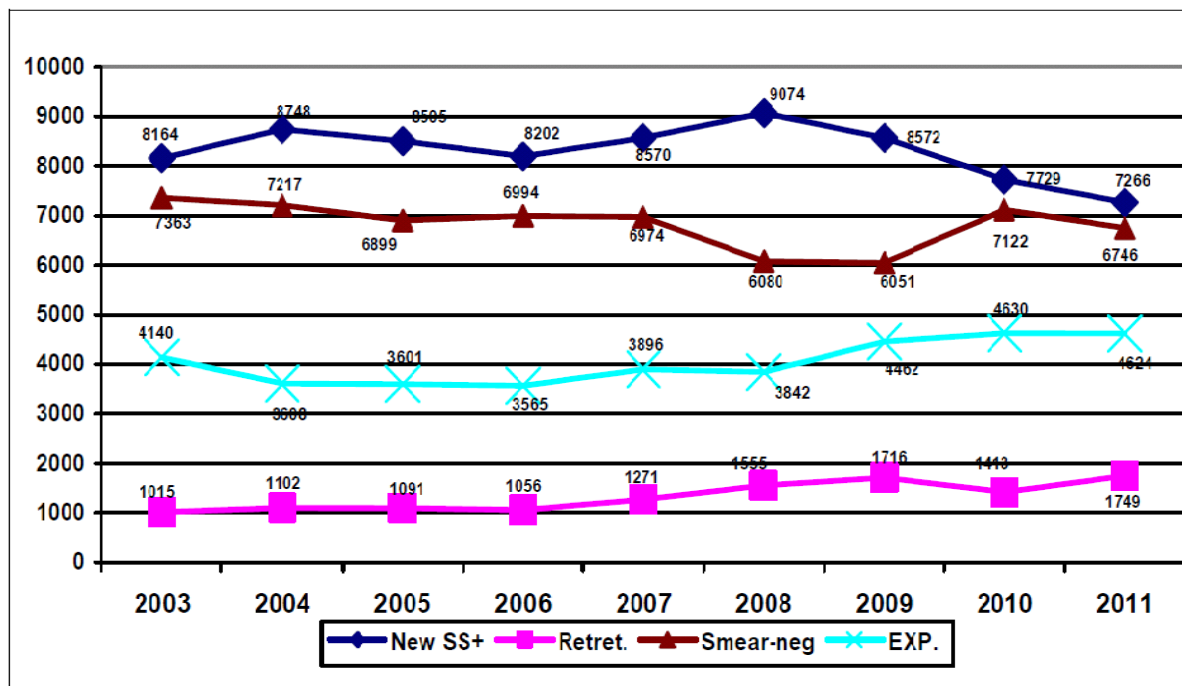
Figure 5: Number of TB cases, Sudan 2007-2011



Data obtained from the Federal Ministry of Health (FMOH) Sudan, Annual Statistical Report, 2011

As shown in figure 6, the number of notified TB cases fluctuated between 2003 and 2011. During that period, new smear positive cases accounted for the highest number followed by, smear negative cases, extra-pulmonary and re-treatment cases respectively (11).

Figure 6: Notified TB cases by category, Sudan 2003-2011



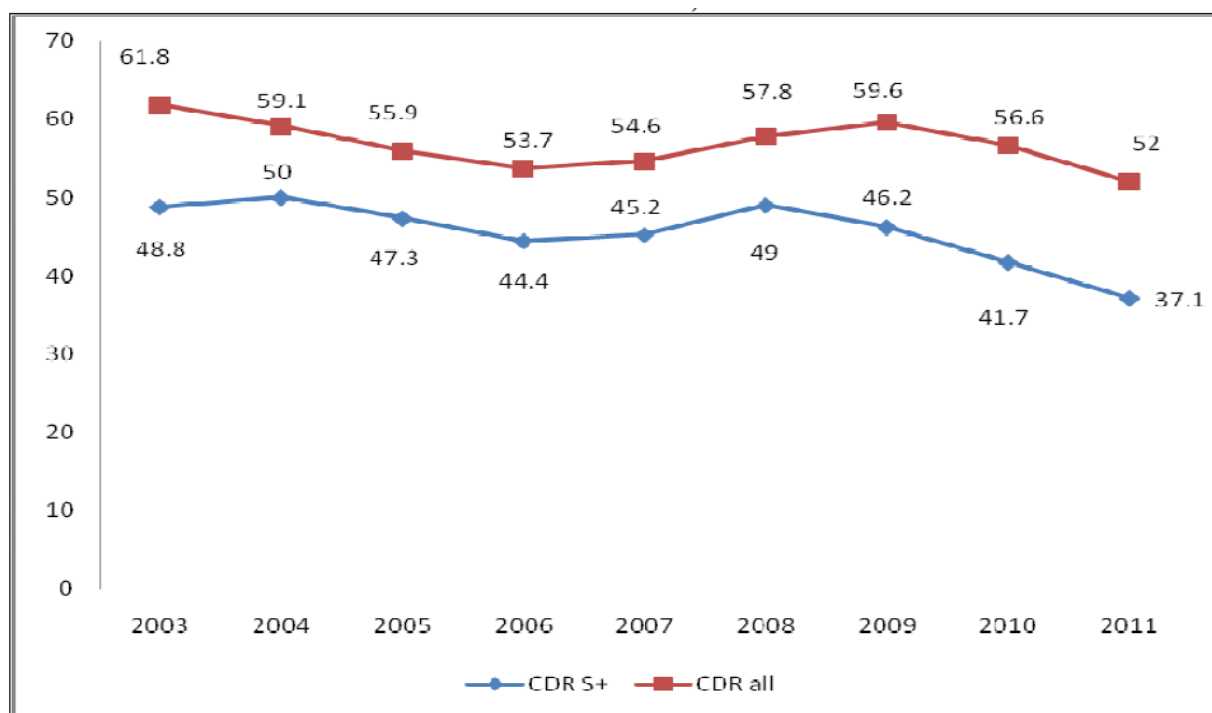
*New SS+: New sputum smear positive, Retret: Retreatment, Smear-neg: Smear negative, EXP: Extra-pulmonary cases

Source: Federal Ministry of Health (FMOH) Sudan, Annual Statistical Report, 2011

Figure 7 and 8, shows the case detection rate and notification rate for TB in Sudan between 2003 and 2011. The case detection rate for all TB cases was slightly reduced from 61.8% in 2003 to 52% in 2011. Similarly, the case detection rate for smear positive cases was reduced from 48.8% to 37.1% during 2003 and 2011 respectively.

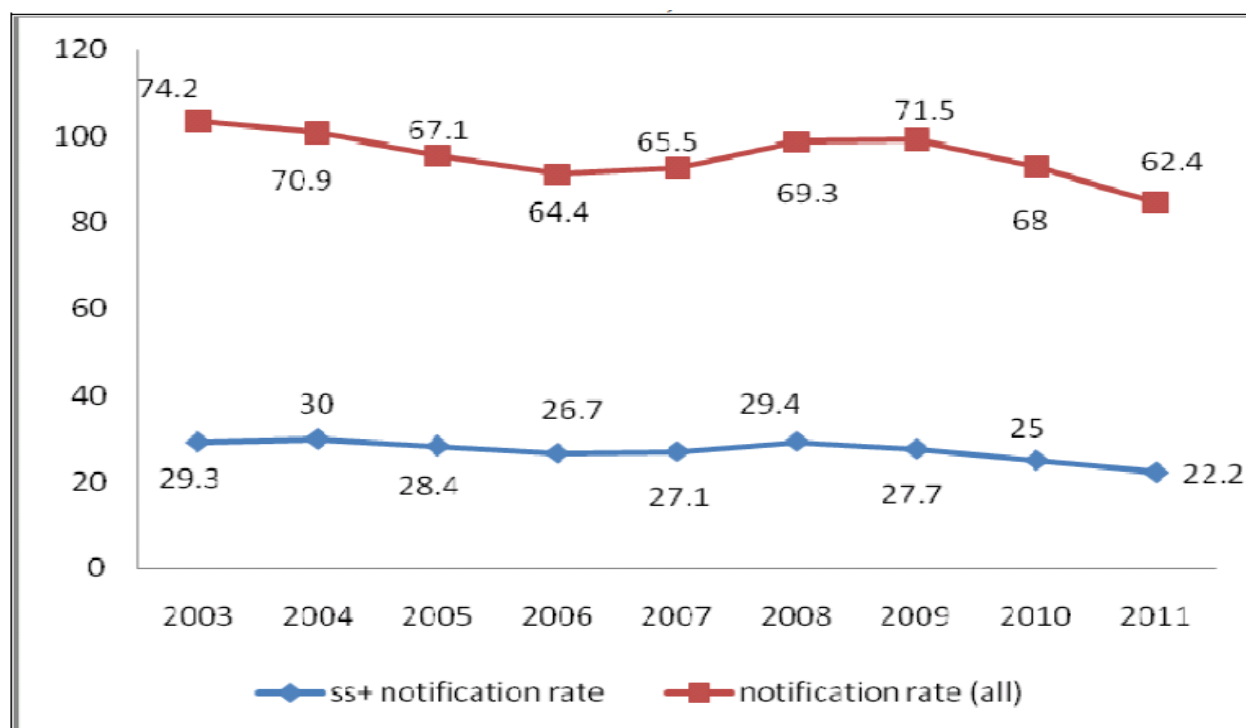
The TB notification rate for all cases showed a slight decline from 74.2% in 2003 to 62.4% in 2011. Similarly the smear positive notification rate dropped from 29.3% in 2003 to 22.2% in 2011.

Figure 7: Case detection rate of TB cases, Sudan 2003-2011



*CDR S+: case detection rate for sputum smear positive cases, CDR all: case detection rate for all TB cases
Source: Federal Ministry of Health (FMOH) Sudan, Annual Statistical Report, 2011

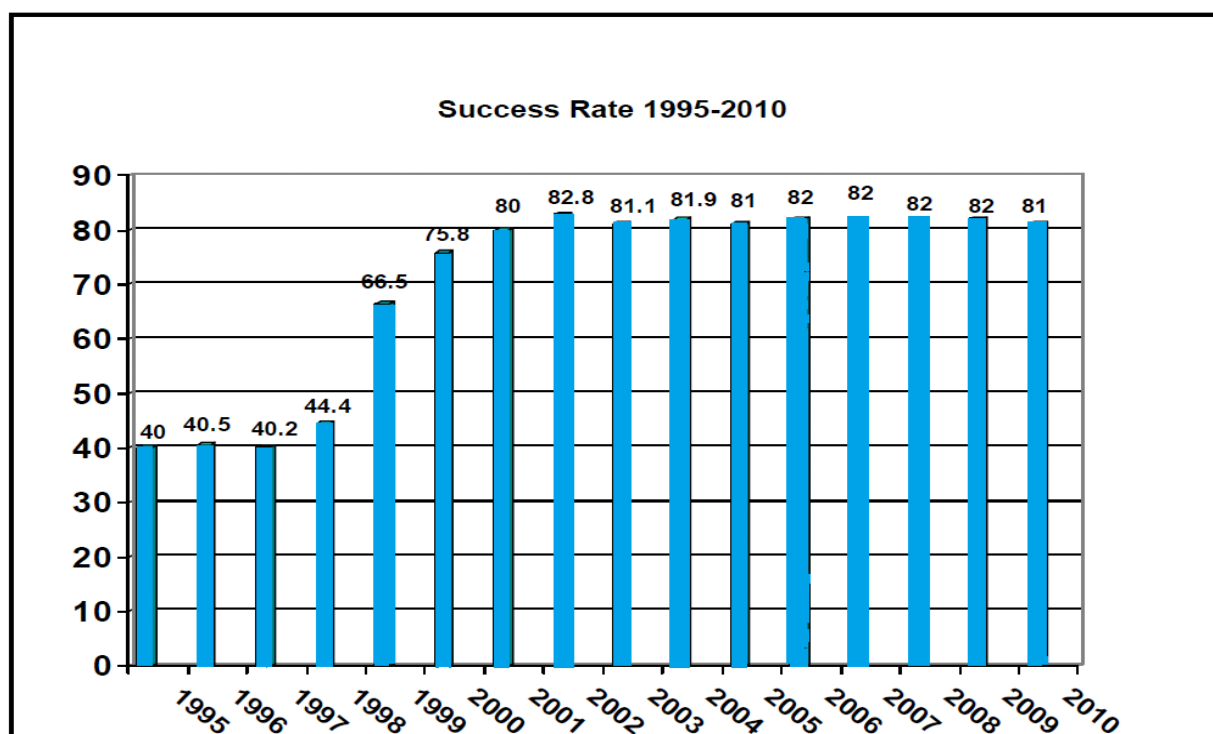
Figure 8: Notification rate of TB cases, Sudan 2003-2011



* SS+: sputum smear positive cases,
Source: Federal Ministry of Health (FMOH) Sudan, Annual Statistical Report, 2011

The treatment success rate, as shown in figure 10, stepped up dramatically from 44 % to 80 % between 1998 and 2000 and remained at this level during 2010. That is most likely due to decentralization of TB services.

Figure 9: Treatment success rate for TB, Sudan 1995-2010



Source: Federal Ministry of Health (FMOH) Sudan, Annual Statistical Report, 2011

Besides the high TB/HIV burden the prevalence of MDR TB is increasing in Sudan. Recently a study reported that, 5% of newly treated, and 24% of previously treated had actually MDR TB, which indicates that Sudan is going to face a serious public health problem, if not properly addressed and handled (45).

3. RATIONALE

In 2004, estimates from the WHO show that there are 64 million people globally suffer from COPD, 3 million people died and 90% of them in low-income countries (2).

Results coming from Latin America (12), suggest that COPD is a greater health problem than previously realized and suggest a high prevalence of COPD in developing countries and particularly in middle income countries which are in similar epidemiologic transition (Asia, North and South Africa).

The morbidity and mortality of COPD are rising worldwide, and the rise is likely to be most dramatic in Asian and African countries over the next two decades due to smoking (17).

Tobacco smoking is an important risk factor for COPD, nonetheless more research is needed to explain relevant risk factors in low and middle income countries where the greatest impact of COPD will occur (46).

As stated previously, not only there is an increasing interest for non-tobacco risk factors, but also there is emerging evidence that PPTB is a risk factor for COPD. However studies conducted on the issue are limited and have some shortcomings. Some relied on self-report as a measure for PPTB while others used PPTB to control for confounding. Some relied on pre-bronchodilator spirometric results rather than the standard definition for COPD (post-bronchodilator $FEV_1/FVC < 0.7$). And some failed to control for important risk factors such as smoking due to lack of data.

Although recently the incidence of TB has been declining worldwide. Sudan is still considered to be one of the high TB burden countries in the Eastern Mediterranean Region (EMRO). Sudan is the third highest TB burden country, together with Afghanistan and Pakistan contribute to 58% of the total cases in the region (47).

The burden of COPD in Sudan is not yet well studied, neither the prevalence nor the risk factors of COPD especially among patients with PPTB.

The aim of this study is to estimate the prevalence and the risk factors of COPD among patients with PPTB in Khartoum state and to assess the association between PPTB and the risk of developing COPD.

4. OBJECTIVES

4.1 General Objective

- To measure the prevalence and risk factors of COPD among past pulmonary tuberculosis (PPTB) patients in Khartoum State, Sudan

4.2 Specific Objectives

- To find out the proportion of COPD cases among treated PPTB patients
- To determine if there is any age difference in response to the development of COPD among treated PPTB patients
- To determine if there is any gender difference in response to the development of COPD among treated PPTB patients
- To identify the effect of smoking on the development of COPD in PPTB patients
- To identify the effect of delayed TB treatment on the development of COPD

5. METHODOLOGY

5.1 The Study Design

This study is a retrospective cross-sectional study aiming to measure the prevalence and risk factors of COPD in PPTB patients in Khartoum State, Sudan.

5.2 The Study Setting

Tuberculosis care is provided by the NTP under the auspices of the MOH and by a number of NGOs who provide care for displaced persons, including those living in refugee camps (43). TB services are provided through 54 Tuberculosis Management Units (TBMUs) as diagnostic and treatment sites and DOTS centers as treatment centers. There are nine federal level units which are specialized chest hospitals or specialized chest units in big hospitals. One of these was selected randomly as the study setting, namely Omdurman teaching hospital.

Omdurman teaching hospital is one of the tertiary hospitals in Khartoum state. The hospital has a capacity of 560 beds for patients' admission and with several specialties including surgery (general, plastic, pediatrics and orthopedics) besides urology and ENT departments. The hospital also provides medical (general, chest, neurology and nephrology) and dentistry services. In addition, the hospital has a referral clinic for all the departments mentioned above. The hospital has an intensive care unit, cardiac care unit, blood bank and a central laboratory unit. Moreover the hospital has 15 medicine consultants and 15 surgery consultants together with a number of registrars, medical officer and house officers.

Daily, approximately 900 to 1000 patients are seen in the outpatient clinics, third of them are patients complaining of chest symptoms. Two thirds of those with respiratory symptoms are asthma patients. The chest referral clinic runs twice per week and approximately 60 patients are seen per clinic. The referral clinic provides a special care for TB and respiratory medicine.

5.3 The Study Duration

Data was collected in the period from July to December 2013. Data entry and analysis and

thesis writing were conducted in the period from January 2014 to May 2014.

5.4 Population and Sampling

5.4.1 Target Population

All adults who are registered in the TB registers (PPTB patients) and their non-TB controls

5.4.2 Study Population

Patients who completed TB treatment at least 5 years ago and their matched non-TB controls

5.4.3 Inclusion criteria

1. Age between 30 to 70 years old.
2. Diagnosed and treated in medical records as PTB patients at least 5 years ago.
3. Presence of valid cell phone on the patient's record to contact the patient.

5.4.4 Exclusion criteria

- 1) Extra pulmonary TB patients
- 2) Smear negative pulmonary TB patients
- 3) Patients who are seriously ill
- 4) Patients with a recent history of
 - Pneumothorax
 - Myocardial infarction or unstable angina
 - Thoracic or abdominal or eye surgery
 - Hemorrhagic cerebrovascular event

5.4.5 Sample Size

This formula was used to determine the sample size (48).

$$N = \frac{\{p1(1-p1)+p2(1-p2)\}}{(p1-p2)^2} \times C_{p, power}$$

Where;

$P1$ and $P2$ are the proportions in the two groups

$C_{p, power}$ is a constant defined by the values chosen for the P value and power, with 80% power using a cutoff for statistical significance of $0.05 = 7.9$

The expected proportion of COPD in PPTB patients is 10%, while for the controls is 2%

Then $n = 0.09 + 0.0196 / 0.0064 \times 7.9 = 135$

Then, the sample size for each group = 135 participants

5.4.6 Sampling Technique

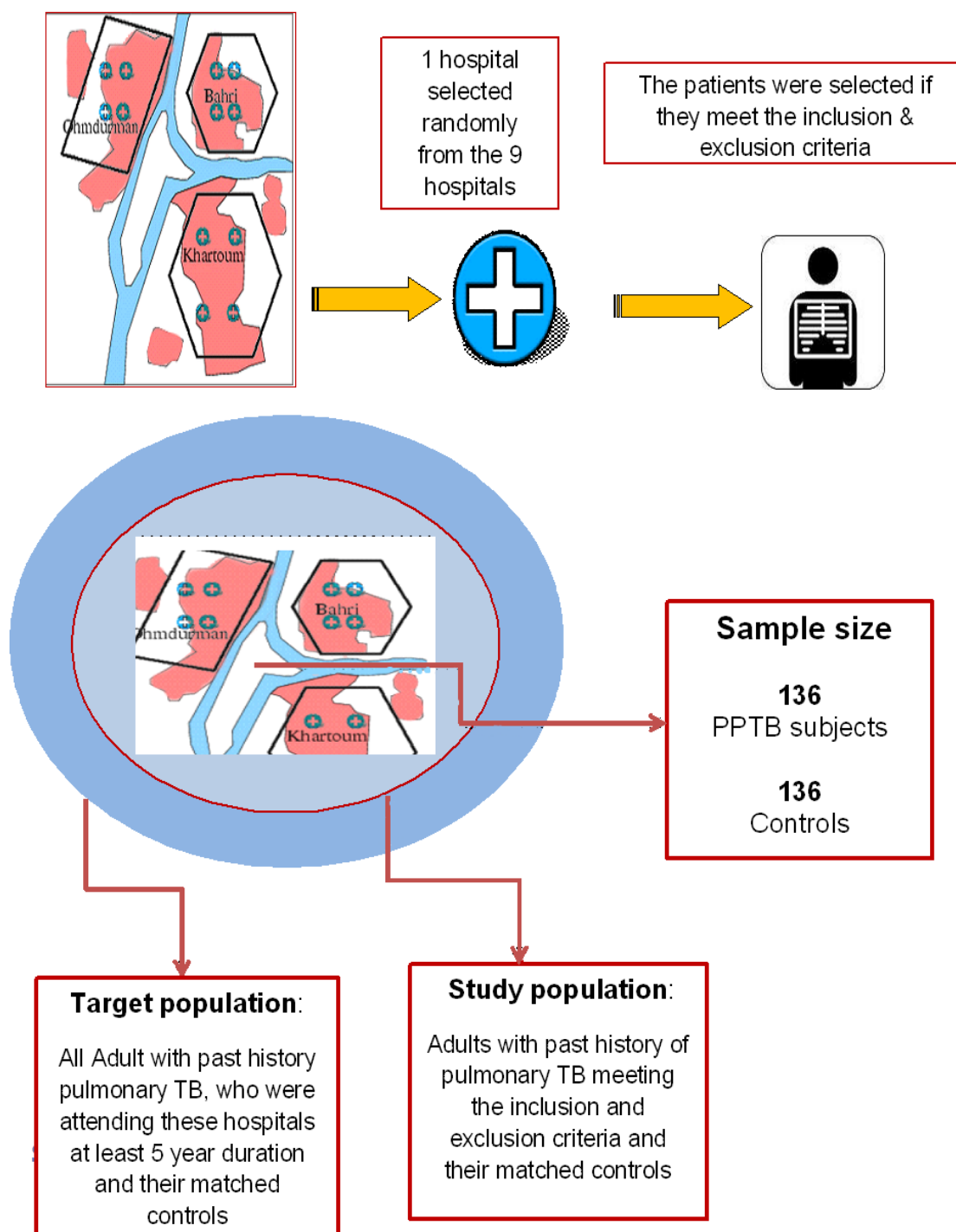
The nine federal hospitals in Khartoum state were stratified geographically; (Khartoum, Omdurman and Khartoum North) one hospital (Omdurman Teaching Hospital) was chosen randomly. From the TB registers of Omdurman hospital, the PPTB subjects were selected conveniently. The relevant subjects were selected from the top of the list and then contacted through phone by the clinic staff. Then they were recruited till the sample needed was met. A matched control by age and sex was invited and recruited from the PPTB subject's relatives, otherwise not fulfilled, a neighbor to the case was invited to participate so as to compare between those who developed COPD and those who did not and to control for confounding factors such as for example; age and sex.

From 2008 and 2009 TB registers, 500 subjects who were identified fulfilling the inclusion criteria. Only 139 subjects were reached by phone and then completed the questionnaires and performed spirometry. Most of the subjects who were contacted were willing to participate and only 5 subjects refused to participate in the study. Fifteen subjects were found to be dead and 31 subjects were out of Khartoum state during the period of the study. Those with unreachable phone were 310 subjects.

No one was excluded because of the exclusion criteria. However, two PPTB subjects were excluded from the study because they were known asthmatic patients with a physician's

diagnosis. Another PPTB subject was excluded because his spirometric curves were technically unsatisfactory. Hence the total number of PPTB subjects enrolled in the study was 136 with equal number of age and sex matched controls.

Figure 10: Sampling technique



5.4.7 Study Variables and Outcomes

The study variables and outcomes are shown in table 1. Treatment outcomes and TB episodes were initially planned to be included in the study, but because of missing data or inconsistency these two variables were not studied.

Table 1: Study variables and outcomes

	Factor	Variable	Indicator	Scale	Method of verification
Independent	Socio-demographic Variables	Age	Years	Numerical	Register records and questionnaire
		Sex	M,F	Categorical	
		Education	Level	Categorical	
		Occupation	Description	Categorical	
		Residence	Place	Categorical	
		Income	Low,Medium,High	Categorical	
		Ethnicity	Description	Categorical	
Independent	Modifiable	Smoking	Yes, No	Categorical	Questionnaire
		Occupational exposure (Dust, gas and chemical fumes)	Yes, No	Categorical	
		Smoke exposure from biomass fuel use	Yes, No	Categorical	
		Comorbidity	Yes, No	Categorical	
		BMI, according to WHO classification (49)	Underweight(<18.5) Normal(18.5-24.9) Overweight(25-30) Obese (>30)	Categorical	Weight and height measurement
Independent	PPTB	Treatment outcome	Indicators	Categorical	Register records and questionnaire
		TB episodes	Number	Numerical	
		Smear results	Positive, Negative	Categorical	
		Treatment delay	Yes, No	Categorical	
Dependent	COPD	Symptoms	Yes, No	Categorical	Questionnaire
		Obstruction	Yes, No	Categorical	Spirometry
		Severity grade, according to GOLD criteria	Mild, Moderate, Severe, Very severe	Categorical	Spirometry

5.5 Data Quality and Management

5.5.1 Data Collection Tool and Measurement

Participants were asked to undergo an interview using a questionnaire after meeting the inclusion and exclusion criteria. The questionnaire was tested and validated for clarity and consistency. Patient's socio-demographic variables and risk factors for COPD were assessed using questionnaires. PPTB and related data were collected from the patient's records except for delayed TB treatment for which the questionnaires were used. Interviews and examinations took place at home for most of the participants, while few opted to be interviewed at Omdurman referral clinic.

After the participants were interviewed using the questionnaires, their height and weight were measured. Subjects were asked to take a deep inhalation and then blow as forcefully and as long as they can three times in the spirometer. The same instructions were given after 15 minutes of taking two puffs twice from a bronchodilator. The best out of three readings was chosen before and after the bronchodilator. A spacer was used for the subjects who were not able to inhale properly, even after they were instructed on how to use the inhaler.

Diagnosis of COPD was established by symptoms and pulmonary function tests using spirometry based on GOLD criteria for COPD diagnosis (1). The diagnosis of COPD was considered in any patient who has symptoms of cough, sputum production, or shortness of breath. Presence of a post-bronchodilator $FEV_1 < 80\%$ of the predicted value in combination with a $FEV_1/FVC < 0.7$ confirms COPD diagnosis. The severity of airflow obstruction was graded according to the GOLD criteria for classification of COPD severity from grade 1 to 4. A variable for airflow obstruction (yes/no) was generated based on the results.

All the study participants completed the pre-bronchodilator tests. However two subjects from the PPTB group and 8 control subjects refused to perform the post-bronchodilator tests (they stated that they do not have any chest symptoms and hence no need for the bronchodilation

test). None of them was found to have airflow obstruction according to their pre-bronchodilator spirometric results.

The lung function tests were performed to the study participants by the researcher after attending a training course on spirometry. All the spirometric tests were conducted using, One Flow FVC # 7880 spirometer (Clement Clarke International, England). While the bronchodilator used was Ventolin (Salbutamol) Inhaler 100 mcg, 200 Doses/Inhaler produced by GlaxoSmithKline.

5.5.2 Data Quality

The questionnaire was pretested before being administered. The questionnaires were then cleaned and corrected for completeness and correctness on site. A double data entry and cross validation was conducted. Every subject was given a single defined code. After the lung function tests were performed using the spirometer, the results appeared in the software program designed especially for the spirometer. The results were checked, verified and interpreted by the researcher and confirmed by chest specialist.

5.5.3 Data Analysis and Management

The chi - square test was used for categorical variables (sex, smoking, education Etc.) and t-test to compare between the means in numerical variables such as age. Linear regression was used to assess the spirometric indices (FEV1, FVC and FEV1/FVC ratio) before and after the bronchodilator. Furthermore, binary logistic regression was used to calculate the odds of having COPD after past exposure to PTB. Univariate analysis was conducted for every variable alone and then statistically significant results ($p < 0.05$) were included together in the multivariate model. The data was entered and analyzed using the Statistical Package for the Social Sciences software (SPSS) version 20. Microsoft Excel and Word were used to generate figures and tables.

5.6 Ethical consideration

5.6.1 Approval

Approval from the relevant ethical review committees was sought from both Norway and Sudan.

5.6.2 Consent

A written informed consent was obtained from the participants after clearly explaining the study objectives to them and ensured that their data will be kept confidential.

5.6.3 Harm and Benefit

The study poses no harm to the participants. Few participants might experience some discomfort associated with spirometry such as dizziness and breathlessness, although, this is uncommon. The spirometry is the standard test of lung function and is performed in patients and normal subjects worldwide. The participants can withdraw at any time during the study period. There are no direct benefits to the participants from participating in this study. The indirect benefit associated with participation in the study include; if a participant showed evidence of airflow obstruction will be benefited from the study by referring him/her to the relevant management facilities for further medical care and advice. Knowledge of their current state of lung function is of value to participants' health.

5.7 Contribution to knowledge

The study aims to provide data about the prevalence and risk factors of COPD among patients with PPTB, and to add to the existing knowledge about COPD and PPTB sequel in one of the lower middle income countries, where the greatest impact of COPD is expected to occur.

5.8 Dissemination of results and publications plan

Results are aimed to be disseminated to Sudan FMOH, Khartoum SMOH, NTP, Communicable and Non-communicable Disease Departments, UIO, national and international journals.

6. RESULTS

The study was mainly conducted aiming to figure out the prevalence and risk factors of COPD among PPTB subjects and to identify the effect of subjects' socio-demographic characteristics and health related factors on the risk of developing COPD. The socio-demographic characteristics and other risk factors were assessed using structured questionnaires. COPD diagnosis was established by using spirometry and symptoms related to airflow obstruction. The results are based on the analysis of 136 PPTB and their controls.

6.1 Response Rate

A total of 139 out of 190 past PTB patients were approached by phone during the study period after meeting the inclusion criteria, and completed the questionnaire and performed spirometry, with a response rate of 73.16 %.

6.2 Socio-demographic Characteristics

6.2.1 Age

The mean age of the study participants was 42.22 ± 8.55 years, a median of 42.50 and with a range of 33 to 66 years. Almost half of the study participants, 117 (43.0%) were in the age group less than 40 years, while 82 (30.1%) were in the age group 40-49 years and 73 (26.8%) are of the age group more than 50 years of age.

6.2.2 Gender

The male to female ratio showed male predominance, almost three quarter of the study participants were males 198 (72.8%) while the females were only 74 (27.2%).

6.2.3 Marital status

A total of 203 (74.6%) of the study participants were married, 26 (17.6%) were singles, 6 (2.2%) were divorced and 15 (5.5%) were widowed.

6.2.4 Education

In regards to education, 26 (9.6%) of the study participants were illiterates, 35 (12.9%) with no formal education, 47 (17.3%) with primary schooling, 91 (33.5%) with secondary schooling and 73 (26.8%) with university and above educational level.

6.2.5 Occupation

Regarding occupation, 13 (4.8%) of the participants were unemployed, 4 (5.1%) were retired, 27 (9.9%) were workers, 51 (18.8%) were employed, while 125 (46.0%) were freelancers and more than two third of the females 52 (19.1%) were housewives.

6.2.6 Monthly Income

In regards to the monthly income, 63 (23.8%) of the study participants were with a monthly income less than 500 Sudanese Pound (SDG), 87 (32.8 %) were within 500-1000 SDG, 81 (30.9%) were within 1001-2000 SDG and 33 (12.5%) were with an income of more than 2000 SDG per month.

6.2.7 Address

Most of the study participants, 213 (78.3%) resided in Omdurman, 30 (11.0%) in Khartoum, and 29 (10.7%) in Khartoum North.

6.2.8 Ethnic Origin

Originally, 83 (30.5%) of the study participants were from the Northern States, 50 (18.4%) from Central Sudan, 63 (23.2%) from Kurdufan, 54 (19.9%) from Darfur, 12 (4.4%) from Blue Nile State, and 10 (3.7%) participants were originally from Eastern Sudan.

6.3 Socio-demographic characteristics and PPTB

The total number of study participants was 272, divided into two equal halves, 136 (50.0%) PPTB cases and 136 (50.0%) controls.

The mean age of the PPTB subjects was 43.97 ± 8.51 years, while for the controls was 44.47 ± 8.61 years (figure 11 and 12). The female to male ratio is equal in both PPTB subjects and controls; 37 (27.2%) to 99 (72.8%) in both groups.

Figure 11: Age of past pulmonary tuberculosis cases in histogram, n= 136

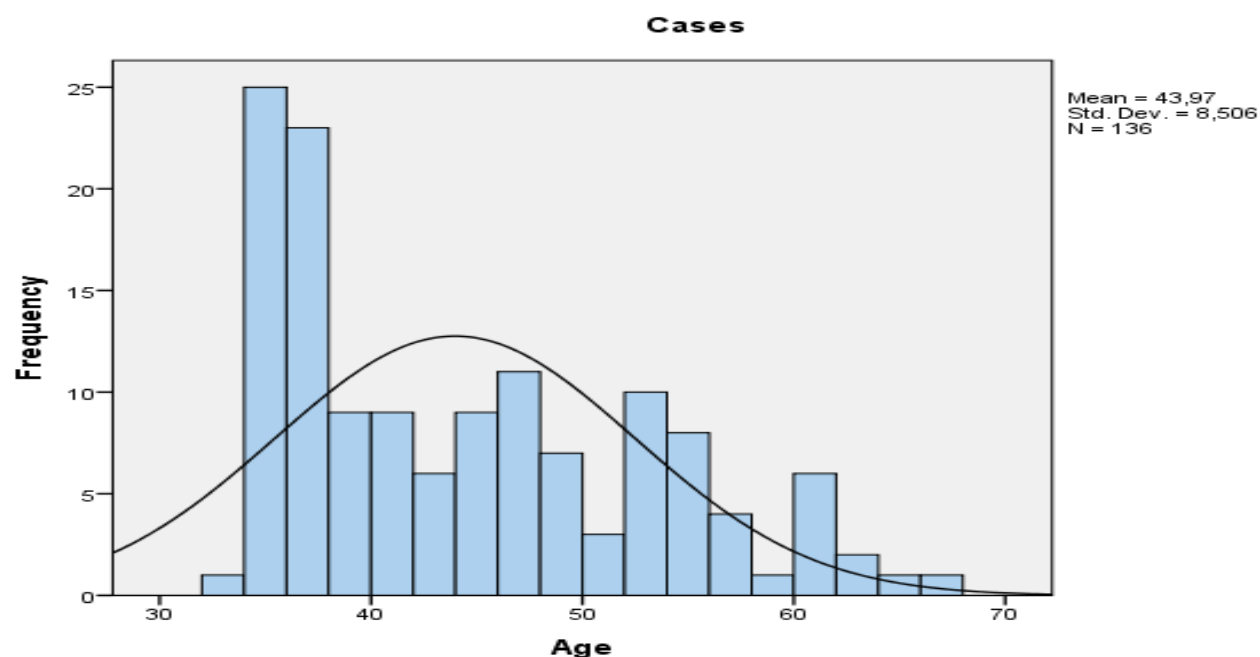


Figure 12: Age of the study controls in Histogram, n= 136

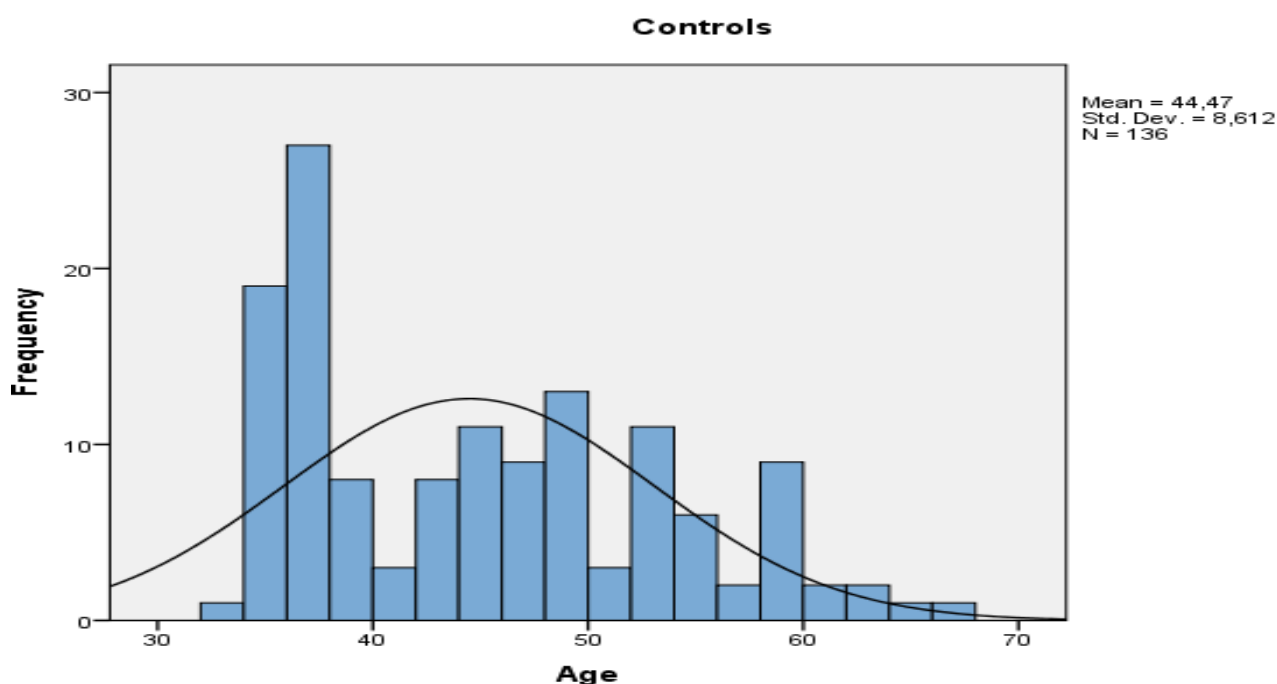


Table 2, describes the associations between the independent variables of socio-demographic characteristics and PPTB. All the variables of the socio-demographic characteristics were not significantly associated with PPTB. There was not a statistically significant difference by being a PPTB subject or a control in regards to age ($P=0.810$), gender ($P=1.000$), marital status ($P=0.414$), education ($P=0.761$), occupation ($P=0.128$), monthly income ($P=0.323$), residence ($P=0.497$), or origin ($P=0.597$).

Table 2: Associations between socio-demographic characteristics and PPTB

		PPTBS* n (%)	Controls n (%)	Total n (%)	p-value[#]
Age	< 40 years	61 (52.1)	56 (47.9)	117 (100)	.810
	40 - 49 years	39 (47.6)	43 (52.4)	82 (100)	
	> 50 years	36 (49.3)	36 (50.7)	73 (100)	
Gender	Female	37 (50.0)	37 (50.0)	74 (100)	1.000
	Male	99 (50.0)	99 (50.0)	198 (100)	
Marital Status	Single	23 (47.9)	25 (52.1)	48 (100)	.414
	Married	100 (49.3)	103 (50.7)	203 (100)	
	Divorced	5 (83.3)	1 (16.7)	6 (100)	
	Widowed	8 (53.3)	7 (46.7)	15 (100)	
Education	Illiterate	14 (53.8)	12 (46.2)	26 (100)	.761
	Non-formal	14 (40.0)	21 (60.0)	35 (100)	
	Primary school	24 (51.1)	23 (48.9)	47 (100)	
	Secondary school	48 (52.7)	43 (47.3)	91 (100)	
	University & above	36 (49.3)	37 (50.7)	73 (100)	
Occupation	Unemployed	10 (76.9)	3 (23.1)	13 (100)	.128
	Retired	4 (100)	0 (0.0)	4 (100)	
	Worker	13 (48.1)	14 (51.9)	27 (100)	
	Employed	26 (51.0)	25 (49.0)	51 (100)	
	Freelancer	58 (46.4)	67 (53.6)	125 (100)	
	Housewife	25 (48.1)	27 (51.9)	52 (100)	
Monthly income	< 500 SDG	35 (55.6)	28 (44.4)	63 (100)	.323
	500 – 1000 SDG	46 (52.9)	41 (47.1)	87 (100)	
	1001 – 2000 SDG	35 (42.7)	41 (57.3)	82 (100)	
	> 2000 SDG	14 (42.4)	19 (57.6)	33 (100)	
Address	Omdurman	107 (50.2)	106 (49.8)	213 (100)	.497
	Khartoum	17 (56.7)	13 (43.3)	30 (100)	
	Khartoum North	12 (41.4)	17 (58.6)	29 (100)	
Origin	North	40 (48.2)	43 (51.8)	83 (100)	.597
	Center & Jazeera	24 (48.0)	26 (52.0)	50 (100)	
	Kurdufan	31 (49.2)	32 (50.8)	63 (100)	
	Darfur	26 (48.1)	28 (51.9)	54 (100)	
	Blue Nile	9 (75.0)	3 (25.0)	12 (100)	
	East	6 (60.0)	4 (40.0)	10 (100)	

PPTBS*: Past pulmonary tuberculosis subjects

P-value[#]: Pearson chi square test or Fischer exact test was used accordingly

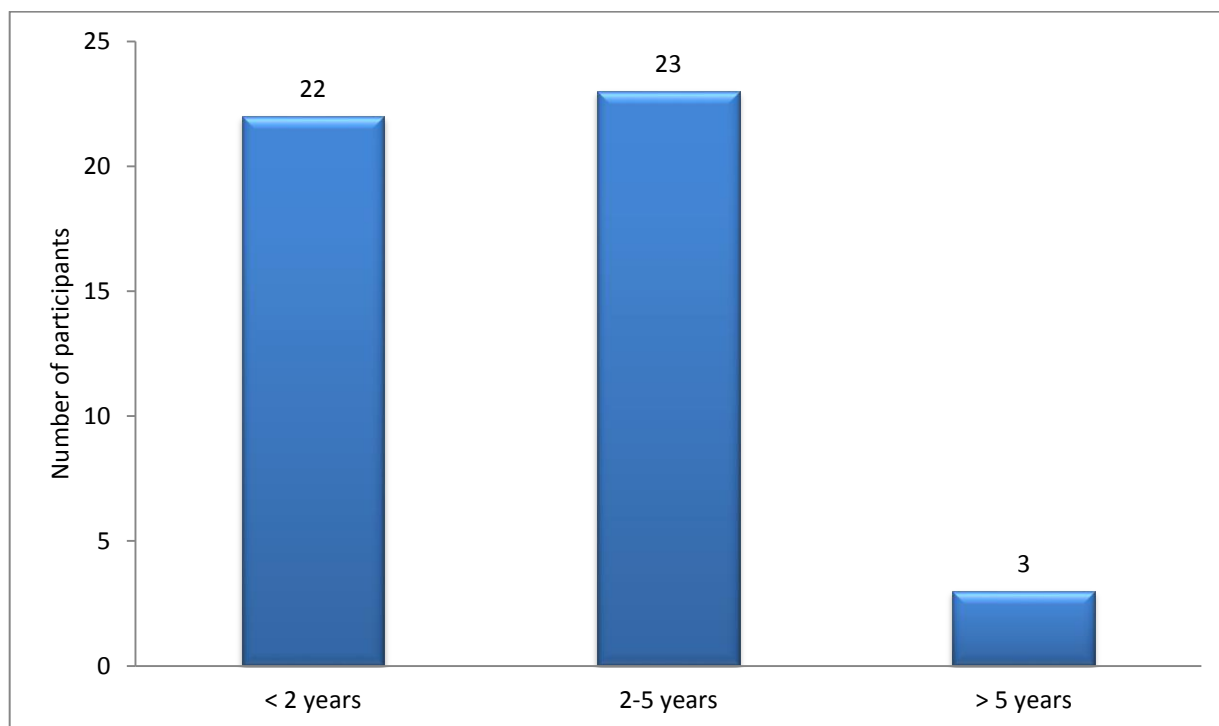
6.4 Health related factors

6.4.1 Respiratory symptoms

6.4.1.1 Cough

Only 48 (17.6%) out of the 272 study participants were having a chronic cough that is not associated with cold, of whom only 18 (37.5%) had this cough in most of the days for 3 consecutive months or more during a year.

Figure 13: Duration of cough



6.4.1.2 Phlegm

Only 44 (16.2%) out of the 272 study participants were bringing up phlegm, of whom only 13 (29.5%) had this phlegm most of the days for 3 consecutive months or more during a year.

Figure 14, shows the duration of phlegm.

6.4.1.3 Wheeze

Only 17 (6.3%) out of the 272 study participants had wheeze for the past year, of whom only 11 (4.0%) had this wheeze without cold and 14 (5.1%) felt shortness of breath when they had the wheeze. Figure 15, shows the duration of wheeze.

Figure 14: Duration of phlegm

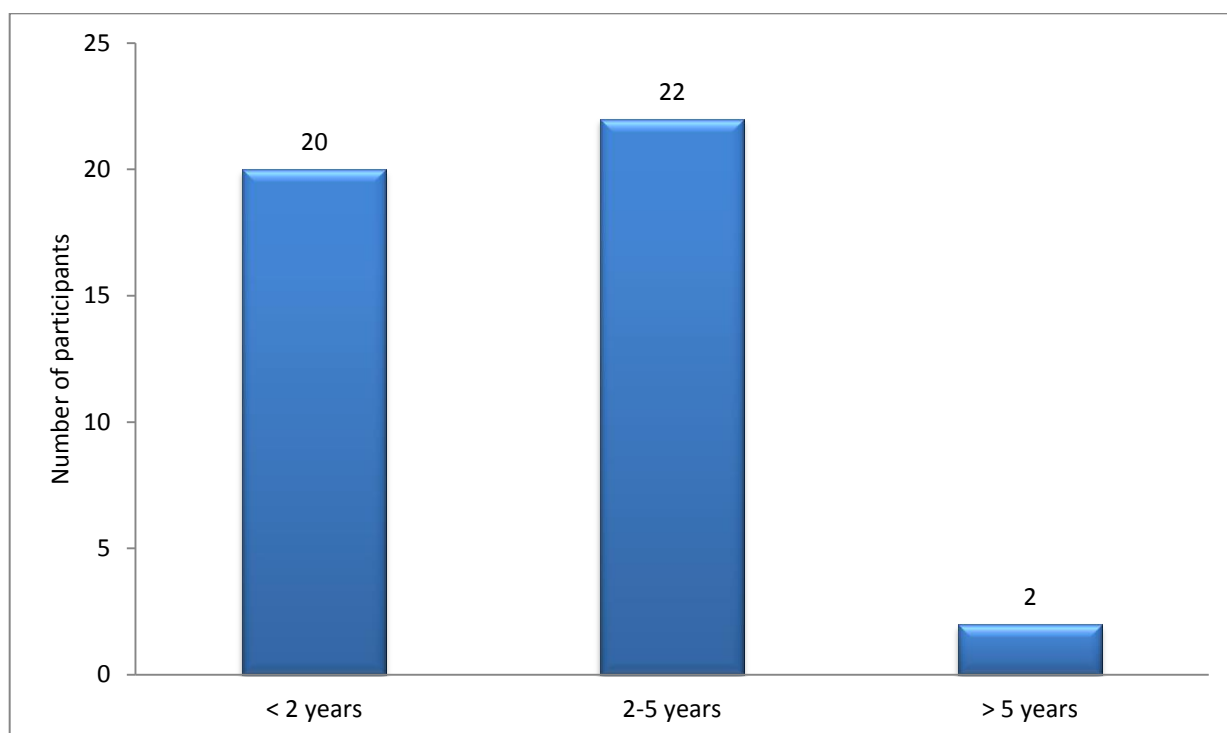
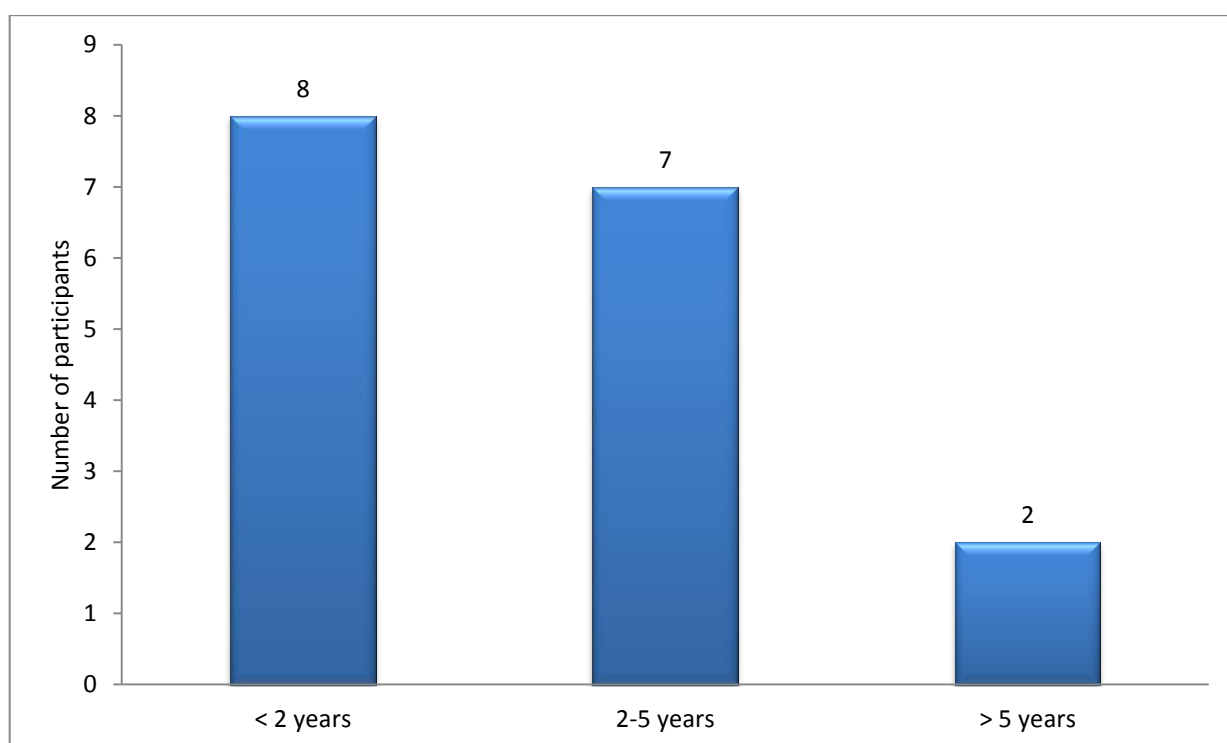


Figure 15: Duration of wheeze



6.4.1.4 Shortness of breath

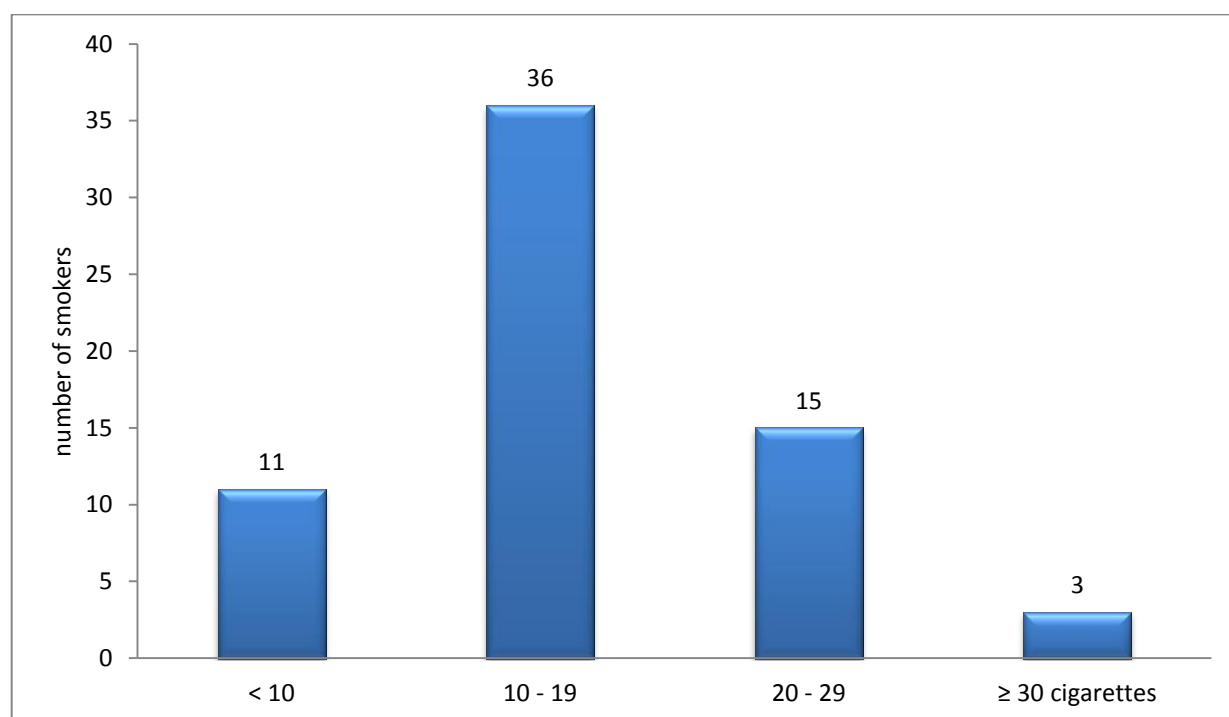
Out of the 272 participants, only 20 (7.4%) had shortness of breath at rest and 52 (21.0%) following strenuous activity during the past year. Only 7 (2.6%) participants had been woken

by shortness of breath, of whom 5 (71.4%) had been woken once and 2 (28.6%) twice during the past 3 months. Furthermore 51 (18.8%) participants were troubled by shortness of breath when hurrying or walking up a slight hill while 15 (5.5%) had to walk slower than the people of their age and only one (0.4%) participant had to stop for breath while walking at own pace on the level. One participant (0.4%) had a diagnosis of chronic bronchitis that was confirmed by a doctor.

6.4.2 Smoking

Out of the 272 study participants, 65 (23.9%) stated that they smoked cigarettes, of whom 24 (36.9%) were currently smokers while 207 (76.1%) had never smoked.

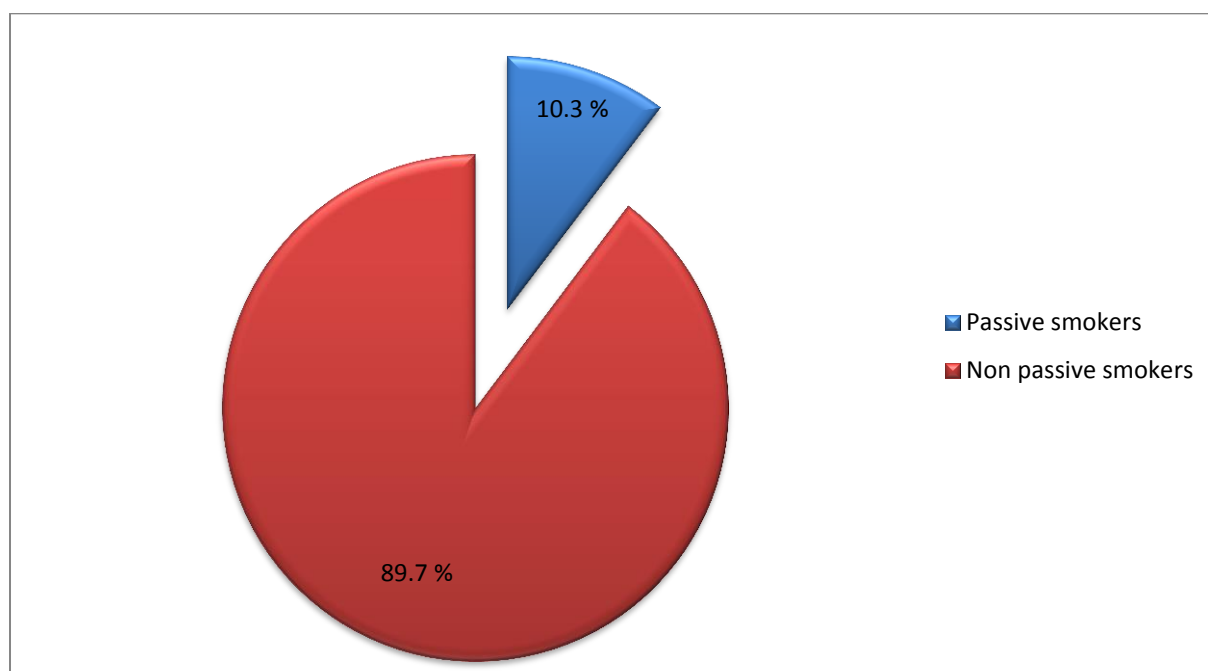
Figure 16: Average number of cigarettes per day smokers used to smoke



In regards to smoking water pipe (*Shisha*) 12 (4.4%) out of the 272 study participants smoked *Shisha*, of whom only 2 (16.7%) were still *Shisha* smokers. The number of *Shisha* smoked per day ranged from 1 to 5 and most of the *Shisha* smokers 9 (81.1%) smoked either once or twice per day.

In regards to passive smoking, out of the 272 study participants only 28 (10.3%) subjects were passive smokers (figure 17).

Figure 17: Passive smokers compared to the non-passive smokers



6.4.3 Chronic comorbidities

Out of the 272 study participants, 47 (17.3%) had chronic comorbidities. Diabetes mellitus was the most frequent comorbidity 19 (40.4%) followed by hypertension 11 (23.4%). HIV/AIDS and ischemic heart disease, had the same representation 6 (12.8%) among all comorbidities. Moreover, there are five participants (1.8%) who had a family history of bronchial asthma.

Table 3: Distribution of comorbidities and their percentages

	Number	Percentage
CRF	1	2.1
CVD	2	4.3
DM	19	40.0
Epilepsy	1	2.1
HIV/AIDS	6	12.8
HTN	11	23.4
IHD	6	12.8
RA	1	2.1
Total	47	100.0

CRF: Chronic renal failure, CVD: Cerebrovascular disease, DM: diabetes mellitus, HIV/AIDS: Human immunodeficiency virus/ Acquired Immunodeficiency Syndrome, HTN: Hypertension, IHD: Ischemic heart disease, RA: Rheumatoid arthritis

6.4.4 Exposure to dust at work

From all the study participants, only 19 (7.0%) had worked for a year or more in a dusty job. Of those exposed to dust during work, 11 (57.9%) subjects had mild exposure, 7 (36.8%) had moderate exposure and only one (5.3%) subject had severe exposure.

Table 4: Distribution of dusty jobs and their percentages

	Number	Percentage
Cartoon factory	1	5.3
Cement factory	2	10.5
Construction	4	21.1
Mill factory	2	10.5
Mining	2	10.5
Soap powder factory	1	5.3
Textile factory	1	5.3
Well digging*	6	31.6
Total	19	100.0

Well digging*: involving any exposure to silica as a result of digging in the dry soil such as water well, holes and confined spaces.

6.4.5 Exposure to gas and chemical fumes

Regarding exposure to gas and chemical fumes at work for a year or more, only 4 (1.5%) from the study participants had been exposed. Of those who were exposed, 3 (75.0%) subjects had mild exposure, only 1 (25.0%) subject had moderate exposure and none had severe exposure. Two subjects had worked in painting, one in diesel and another one as a welder.

6.4.6 Biomass smoke exposure

Exposure to smoke from the use of biomass for heating or cooking presented in 57 (21%) subjects out of the total sample.

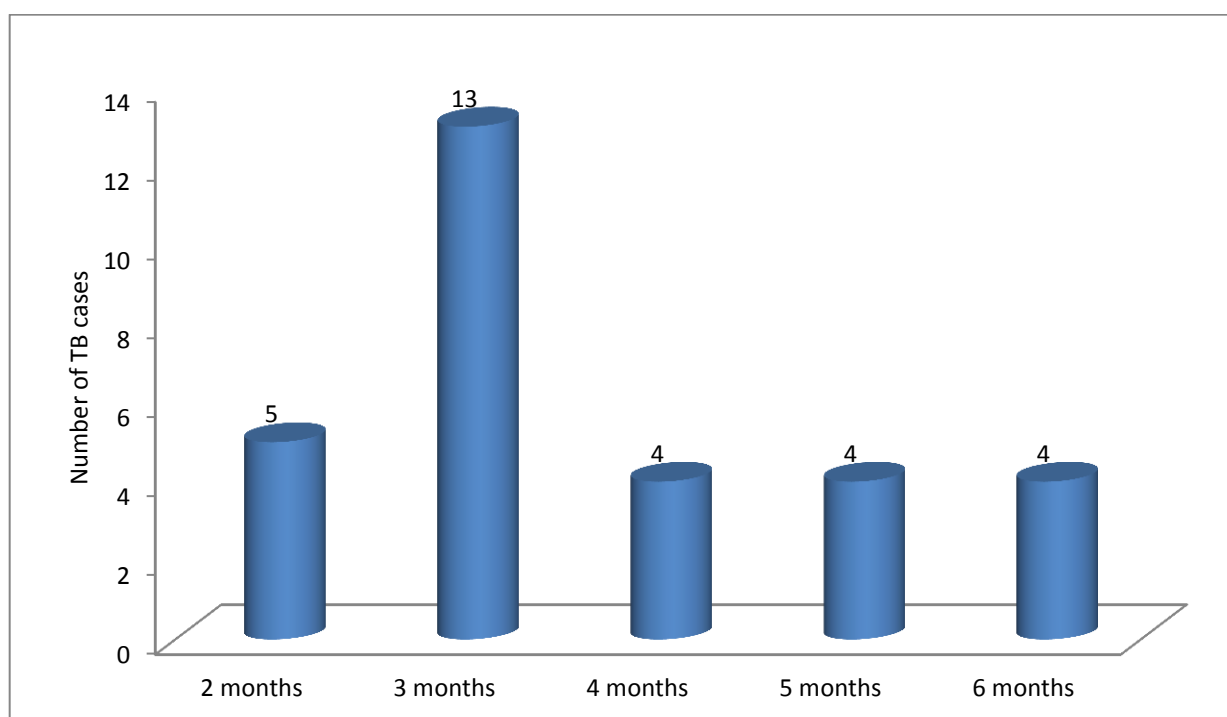
6.4.7 Body Mass Index (BMI)

According to BMI levels, more than half of the study subjects 152 (55.9%) were within the normal range, 93 (34.6%) were overweight, 18 (6.6%) were underweight and only 8 (2.9%) were obese.

6.4.8 Delayed tuberculosis diagnosis and treatment

Out of the 136 PPTB subjects, 30 (22.1%) stated that they had delayed treatment. Those who have delayed treatment stated the reasons as, late diagnosis accounting for 15 (50.0%), followed by use of traditional medicine, accounting for 10 (33.3%), financial reasons accounting for 2 (6.7%), social reasons accounting for 2 (6.7%), and negligence accounting for only one (3.3%) subject.

Figure 18: Time between TB symptoms appearance and starting treatment



6.5 Health related factors and PPTB

6.5.1 Symptoms and PPTB

As table 5 describes, the associations between the symptoms and PPTB, there was a statistically significant difference between the PPTB subjects and the controls in most of the symptoms.

Cough ($P < .001$), phlegm ($P < .001$), and wheeze ($P = .002$), were associated significantly with PPTB. In addition, PPTB was also significantly associated with shortness of breath in most of its severity forms except for waking up by shortness of breath ($P = .120$) and stopping for breath while walking on pace ($P = 1.000$).

Table 5: Association between chronic respiratory symptoms and PPTB

		PPTBS N (%)	Controls N (%)	Total N (%)	p-value
Do you usually have cough that is not associated with cold?	Yes	40 (83.3)	8 (16.7)	48 (100)	<.001
	No	96 (42.9)	128 (57.1)	224(100)	
Do you usually bring up phlegm from your chest?	Yes	37 (84.1)	7 (15.9)	44 (100)	<.001
	No	99 (43.4)	129 (56.6)	228 (100)	
Do you have wheeze or whistling sound in your chest for the past year?	Yes	15 (88.2)	2 (11.8)	17 (100)	.002
	No	121 (47.5)	134 (52.5)	255 (100)	
Have you ever had an episode of wheeze and shortness of breath?	Yes	23 (82.1)	5 (17.9)	28 (100)	<.001
	No	113 (46.3)	131 (53.7)	244 (100)	
Have you had shortness breath while at rest of during the past year?	Yes	19 (95.0)	1 (5.0)	20 (100)	<.001
	No	117 (46.4)	135 (53.6)	252 (100)	
Have you had shortness breath following strenuous activity during the past year?	Yes	51 (89.5)	6 (10.5)	57 (100)	<.001
	No	85 (39.5)	130 (60.5)	215 (100)	
Have you been woken by shortness of breath during the past 3 months?	Yes	6 (85.7)	1 (14.3)	7 (100)	.120
	No	130 (49.1)	135 (50.9)	265 (100)	
Are you troubled by shortness of breath when hurrying or walking up slight hill?	Yes	43 (84.3)	8 (15.7)	51 (100)	<.001
	No	93 (42.1)	128 (57.9)	221 (100)	
Do you have to walk slower than people of your age on the level because of breathlessness?	Yes	15 (100.0)	0 (0.0)	15 (100)	<.001
	No	121 (47.1)	136 (52.9)	257 (100)	
Do you have to stop for breath when walking at your own pace on the level?	Yes	1 (100.0)	0 (0.0)	1 (100)	1.000
	No	135 (49.8)	136 (50.2)	271 (100)	

PPTBS*: Past pulmonary tuberculosis subjects

P-value[#]: Pearson chi square test or Fischer exact test was used accordingly

6.5.2 Smoking and PPTB

There was not a statistically significant association between cigarette smoking ($P=.477$), *Shisha* smoking ($P=.137$), or passive smoking ($P=.690$) with PPTB.

Table 6: Association between smoking and PPTB

		PPTBS* N (%)	Controls N (%)	Total N (%)	p-value [#]
Have you ever smoked cigarettes?	Yes	35 (53.8)	30 (46.2)	65 (100)	.477
	No	101 (48.8)	106 (51.2)	207 (100)	
Have you ever smoked Shisha?	Yes	9 (75.0)	3 (25.0)	12 (100)	.137
	No	127 (48.8)	133 (51.2)	260 (100)	
Have you ever lived with a smoker?	Yes	15 (53.6)	13 (46.4)	28 (100)	.690
	No	121 (49.6)	123 (50.4)	244 (100)	

PPTBS*: Past pulmonary tuberculosis subjects

P-value[#]: Pearson chi square test or Fischer exact test was used accordingly

6.5.3 Occupational exposure and PPTB

PPTB was significantly associated with exposure to dust ($P=.015$), in contrast to exposure to gas or chemical fumes ($P=.622$) at work.

Table 7: Association between occupational exposures and PPTB

		PPTBS* N (%)	Controls N (%)	Total N (%)	p-value [#]
Have you ever worked for a year or more in any dusty job?	Yes	15 (78.9)	4 (21.1)	19 (100)	.015
	No	121 (47.8)	132 (52.2)	253 (100)	
Have you ever been exposed to gas or chemical fumes at work?	Yes	3 (75.0)	1 (25.0)	4 (100)	.622
	No	133 (49.6)	135 (50.4)	268 (100)	

PPTBS*: Past pulmonary tuberculosis subjects

P-value[#]: Pearson chi square test or Fischer exact test was used accordingly

6.5.4 Exposure to biomass smoke and PPTB

The association between exposure to smoke from biomass for heating or cooking and PPTB was statistically significant ($P=.025$).

6.5.5 Chronic conditions and PPTB

The association between having a chronic illness and PPTB was statistically significant ($P=.034$).

6.5.6 BMI and PPTB

There was not a statistically significant association between BMI ($P=.366$) and PPTB.

Table 8: Association between BMI and PPTB

		PPTBS* N (%)	Controls N (%)	Total N (%)	p-value[#]
Body Mass Index (BMI)	Underweight	12 (66.7)	6 (33.3)	18 (100)	.366
	Normal	78 (51.3)	74 (48.7)	152 (100)	
	Overweight	42 (44.7)	52 (55.3)	94 (100)	
	Obese	4 (50.0)	4 (50.0)	8 (100)	

PPTBS*: Past pulmonary tuberculosis subjects

P-value[#]: Pearson chi square test or Fischer exact test was used accordingly

6.6 Airflow obstruction

Airflow obstruction was diagnosed in 13 (4.8%) out of the total study participants.

Out of 136 PPTB subjects only, 12 (8.8%) were diagnosed with airflow obstruction. Hence the prevalence of airflow obstruction in subjects with PPTB was 8.8%

Furthermore, the association between PPTB and airflow obstruction was statistically significant ($P=.001$).

Table 9: Association between airflow obstruction and PPTB

		PPTBS* N (%)	Controls N (%)	Total N (%)	p-value[#]
Airflow obstruction (COPD)	Yes	12 (92.3)	1 (7.7)	13 (100)	.001
	No	124 (47.9)	135 (52.1)	259 (100)	

PPTBS*: Past pulmonary tuberculosis subjects

P-value[#]: Fischer exact test was used for

In PPTB subjects, 8 subjects had a combined obstructive restrictive pattern while 4 had purely obstructive condition.

Moreover, the severity grades of COPD among subjects with PPTB was 8.3% for mild, 58.3% for moderate, 16.7 % for both severe and very severe grades of obstruction according to the GOLD criteria.

In the PPTB subjects, 6 (20.0%) out of 30 had delayed treatment and the association between delayed treatment and airflow obstruction was statistically significant (P=.014).

Table 10: Association between delayed TB treatment and airflow obstruction

		Obstruction N (%)	No-obstruction N (%)	Total N (%)	p-value
Delayed TB treatment	Yes	6 (20.0)	24 (80.0)	30 (100)	.014
	No	6 (5.7)	100 (91.2)	106 (100)	

6.7 Spirometric results

Table 11, shows the spirometric results of PPTB subjects compared to controls using the linear regression. All the spirometric indices before and after bronchodilator showed that, those with PPTB performed less well than the controls. There were significant differences in the indices between the PPTB group and the control, except for FEV1/FVC ratio in the pre-bronchodilator test.

Table 11: Differences in spirometric results of PPTB subjects compared to controls

	PPTBs		Controls		p-value
	Estimate	95% CI	Estimate	95% CI	
FEV1 pre-BD	2.57	(2.46 - 2.69)	2.95	(2.87- 3.03)	<.001
FEV1 pre-BD % pred	71.75	(68.97- 74.53)	83.92	(82.12- 85.73)	<.001
FVC pre-BD	2.72	(2.60 - 2.84)	3.13	(3.03- 3.23)	<.001
FVC pre-BD % pred	63.29	(60.70 - 65.88)	73.68	(71.44 -75.92)	<.001
FEV1/FVC pre-BD	94.46	(92.58 - 96.34)	95.35	(94.02 - 96.69)	.450
FEV1/FVC pre-BD % pred	118.56	(116.19 -120.93)	119.77	(118.01 - 121.53)	.421
FEV1 post-BD	2.72	(2.62 - 2.82)	3.04	(2.97 - 3.11)	<.001
FEV1 post-BD % pred	76.26	(73.76 - 78.77)	86.99	(85.26 - 88.72)	<.001
FVC post-BD	2.96	(2.86 - 3.06)	3.21	(3.12 - 3.29)	<.001
FVC post-BD % pred	69.05	(67.06 -71.04)	76.13	(74.23 - 78.03)	<.001
FEV1/FVC post-BD	91.86	(89.65 - 94.07)	95.27	(94.06 - 96.49)	.009
FEV1/FVC post-BD % pred	115.33	(112.60 - 118.06)	119.71	(118.06 -121.36)	.008

FEV1: forced expiratory volume in one second, BD: bronchodilator, FVC: forced vital capacity, pred: predicted

6.8 The risk of COPD

Table 12, shows the odds ratio (OR) and the 95 % confidence interval for both the univariate and multivariate logistic regression model. An OR that is above 1 shows an increase in the risk of COPD whereas an OR less than 1 shows a decrease in the risk of COPD. Results that were statistically significant ($p < 0.05$) in the univariate model were also presented in the multivariate model.

Table 12: Logistic regression model for the risk of COPD

		Univariate Analysis		Multivariate Analysis	
Covariates		OR (95 % CI)	P-value	OR (95 % CI)	P-value
Type	Control				
	PPTB*	13.07 (1.67 - 101.94)	0.01	12.39 (1.56 - 98.40)	0.02
Gender	Female				
	Male	0.79 (0.21 - 2.97)	0.73		
Age	<40 years				
	40-49	0.56 (0.11 - 2.96)	0.50	0.60 (0.11 - 3.23)	0.55
	50-59	0.82 (0.15 - 4.33)	0.81	0.91 (0.17 - 4.98)	0.92
	≥ 60	7.47 (1.76 - 31.62)	0.01	7.23 (1.58 - 33.01)	0.01
Salary	<500 SDG				
	500- 1000	0.71 (0.20 - 2.56)	0.60		
	1001-2000	0.14 (0.02 - 1.26)	0.08		
	>2000	0.36 (0.04 - 3.24)	0.36		
Education	No Formal				
	Primary	2.01 (0.32 - 12.56)	0.46		
	Secondary	1.36 (0.24 - 7.65)	0.73		
	University and above	1.71 (0.30 - 9.67)	0.54		
Residence	Omdurman				
	Khartoum	0.70 (0.09 - 5.67)	0.74		
	Khartoum North	1.50 (0.31 - 7.23)	0.61		
Treatment[#]	Early				
	Delayed	4.17 (1.24 - 14.06)	0.02	4.09 (1.17 - 14.32)	0.03
Smoking	No				
	Yes	1.44 (0.43 - 4.85)	0.55		
Biomass use	No				
	Yes	1.73 (0.51 - 5.83)	0.38		
Comorbidity	No				
	Yes	2.23 (0.66 - 7.58)	0.20		
Work exposure	No				
	Yes	2.59 (0.53 - 12.63)	0.24		
BMI	Underweight				
	Normal	0.33 (0.06 – 1.77)	0.20		
	Overweight	0.36 (0.60 – 2.11)	0.26		
	Obese	1.14 (0.09 – 14.78)	0.92		

PPTBS*: past pulmonary tuberculosis patients, SDG: Sudanese pound, BMI: Body mass index

Treatment[#]: the estimates are for the PPTB subjects only

Reference group: first in any of the categorical variables

The risk of COPD in subjects with PPTB was 12.39 times higher than the controls [OR=12.39 (95 % CI 1.56, 98.40)].

Subjects who were at least 60 years were at higher risk of COPD than subjects in the age group < 40 years [OR=7.23 (95 % CI 1.58, 33.01)].

PPTB subjects who have delayed treatment were 4.09 times at higher risk than those who received treatment early [OR=4.09 (95% CI 1.17, 14.32)]

The effect of smoking was also assessed as shown in the univariate analysis, however it was not significant.

Other socio-demographic predictors such as gender, salary, education and residence were also estimated, however none of them was significant in the univariate analysis.

Ethnicity and occupation were also assessed, not shown in the table, because they were not significant and redundant due to lack of subjects in some of their sub-category.

Exposure to smoke from biomass use, occupational exposure, comorbidity and BMI were also estimated, but none of them was significant as shown in the univariate analysis.

7. DISCUSSION

This is to our knowledge the first study to assess the prevalence and risk factors of COPD in PPTB subjects in Sudan. The results are based on 136 PPTB subjects who had the disease five years ago, compared to their age and sex matched community controls. In Omdurman teaching hospital the PPTB subjects were selected from the TB registers of the chest reference clinic and then contacted and enrolled in the study according to the inclusion criteria. By selecting the PPTB subjects, the diagnosis of TB was confirmed by their positive sputum smear results and hence relied on an objective diagnosis rather than self-report TB. The response rate was 73.16 %.

The discussion is concentrated on two comparisons. Firstly, the comparison between the PPTB and the controls, and secondly the comparison between COPD and no COPD in relation to PPTB. There are a number of study findings that merit discussion.

The findings of the study on the socio-demographic characteristics showed that the mean age of the study participants was 42.22 ± 8.55 years. Forty three percent of the study participants were in the age group (less than 40 yrs.). Noteworthy; this age group is the most economically productive one and also the one most affected by TB (5). The male to female ratio was 2.7 showing a male predominance. This is likely due to the fact that TB is more common in men than women (5). This ratio is consistent with another study conducted on MDR TB in Khartoum state (45) reporting a ratio of 2.8. However the male to female ratio globally is 1.9 according to recent estimates (5). Generally, as shown from the results, most of the study participants had a low educational background and socioeconomic status. For instance the participants with higher education and higher income represented only 26.8% and 12.5 % of the study sample respectively.

When PPTB subjects were compared to their controls in regards to all the socio-demographic variables assessed in the study. No statistically significant difference was observed. A finding,

reported earlier by Menezes and his colleagues (18) with regards to gender, education, and ethnicity except for age where there was a significant difference between those who had PPTB and those had not.

In regards to respiratory symptoms, in the present study the overall prevalence of chronic cough, phlegm and wheeze was 17.6%, 16.2%, and 6.3% respectively. The prevalence of shortness of breath varied according to severity ranging from 7.4% at rest up to 21 % following strenuous activity. Chronic respiratory symptoms were significantly more prevalent in PPTB subjects than in the control group; chronic cough ($P<.001$), phlegm ($P<.001$), and wheeze ($P=.002$). In addition, PPTB was also significantly associated with shortness of breath in most of its severity forms. In their review of South African studies, Ehrlich and his colleagues (21) demonstrated that there was an increasing prevalence of respiratory symptoms among those with PPTB compared to those without. In addition, it was observed that most of the odds ratios exceeded 2 and in some cases, they reached very high values (21). Moreover the review reported that the association between PPTB and cough and phlegm was highly consistent. However, the association was less consistent with regards to asthma when defined as recent attacks or nocturnal waking with shortness of breath and chest tightness (21).

In regards to cigarette smoking in the present study, the prevalence of ever smoking was 23.9%, while for water pipe (*Shisha*) was only 4.4% among the study participants. Furthermore, the prevalence of passive smoking was 10.3% among the study participants. A huge difference was observed between men and women (32.3% - 1.4%) in regards to cigarette smoking. A similar trend though with higher proportions when compared to the estimated prevalence among Sudanese adults (24.7% - 2.9%) that was published by the WHO in 2012 (50). There was no statistically significant difference between PPTB subjects and controls in regards to cigarette smoking ($P=.477$). A similar finding was reported earlier by Menezes et al (18), in regards to the differences between those who had PPTB compared to those without, also when smoking was categorized by pack-year.

The prevalence of exposure to smoke from the use of biomass for heating or cooking was 21% in the total sample. This exposure was much higher in women 45.9% than in men 11.6%. Concerning the difference between the two groups in regards to smoke exposure from biomass use, a statistically significant difference was found between the PPTB subjects and their controls ($P=.025$), similar to the study from Latin America (18). Many studies have discussed the association between TB and exposure to biomass fuel; however there are not enough studies in order to clearly state that exposure to smoke from biomass is a risk factor for developing TB (51).

The prevalence of dust exposure at work was 7.0%, while exposure to gas or chemical fumes was 1.5 %. There was a statistically significant difference between PPTB subjects and controls in regards to exposure to dust at work ($P=.015$). This finding was also similar to what was reported by Menezes et al from Latin America (18). However, in regards to exposure to gas or chemical fumes at work in this study, there was no statistically significant difference between PPTB subjects and controls ($P=.622$).

Concerning chronic comorbidities in this study, 17.3% had chronic morbidities with diabetes mellitus being the most frequent comorbidity followed by hypertension, HIV/AIDS and ischemic heart disease. There was a statistically significant difference between PPTB subjects and controls in regards to having a chronic illness ($P=.034$). Earlier studies have reported similar findings. In their study lee et al (20) found that the most common underlying comorbidities were diabetes and malignancy. Menezes et al (18) reported a significant association between medical diagnosis of hypertension and PPTB, whereas diabetes was not significantly associated with PPTB.

With regards to BMI there was no statistically significant difference between the PPTB group and the controls ($P=.366$) a finding similar to what was reported from Latin America (18).

One important finding from this study is that, the association between PPTB and COPD was statistically significant ($P=.001$). Moreover, the prevalence of COPD, among PPTB subjects

was 8.8%. COPD was defined in this study as a FEV1/FVC ratio < 0.7 after post-bronchodilator spirometric test results.

Studies involving active PTB patients have suggested earlier that some of these patients had airflow obstruction and according to two studies, airflow obstruction among active PTB patients varied from 28% (52) to 68% (24). However, recent results coming from different parts of the world suggest that there is an association between PPTB and COPD.

In the present study, prevalence of COPD among PPTB subjects resembles the estimates coming from Asia ranging from 6.5% in China (19), 7.6 % in Taiwan (20) to 10.6 % in the Philippines (53). In South Africa the prevalence of chronic bronchitis among PPTB patients was higher than that observed in our study. In South Africa the prevalence varied according to gender, for males 14.7%, while for females 18.3% (54). This is likely because airflow obstruction was defined based on the presence of chronic productive cough, a different definition from that was used in our study relying on spirometric test results.

A higher prevalence was recorded in Colombia (55). In five different cities, the prevalence of COPD among PPTB subjects was 25.8%, defined by post-bronchodilator FEV1/FVC < 0.7 . Using the same definition of COPD, the highest prevalence was reported from a large population based study in five Latin American cities as 30.7% among PPTB subjects (18).

Another major finding from the present study is that, PPTB was an independent risk factor for COPD, the risk of COPD in PPTB group was 13.07 (95% CI 1.67-101.94) higher than in the control group. The OR dropped slightly to 12.39 (95% CI 1.56 - 98.40) after adjustment for the main risk factors such as age, gender, socioeconomic status, smoking, occupational exposure, exposure to smoke from biomass fuel and BMI. Furthermore, PPTB was the strongest predictor for COPD in this study. Whereas smoking was not a significant risk factor and did not alter the risk of COPD in PPTB subjects.

Most of the preceding studies reported that, there is an increased risk of COPD in PPTB

patients. Our findings, has truly supported the growing evidence on the increased risk of COPD after PTB. In the review of South African occupational and population based studies, Ehrlich et.al (21) documented an OR of 2.6–8.9, depending on the definition of COPD used in the different studies reviewed. For instance the strongest predictor of COPD was a history of PTB with an OR of 4.9 (95% CI 2.6-9.2) for males and 6.6 (95% CI 3.7-11.9) for females among South African adults (54), additionally the association was stronger for TB than for tobacco smoking or exposure to smoke from biomass fuel. Also in another study from South Africa the strongest association with COPD was for TB and the OR ranged from 7.7 to 8.1 adjusted for age, gender, smoking status and occupational exposure (56).

This finding was further supported by the findings from Colombia (55), reporting higher odds for TB 2.94 (95% CI 1.6-5.5) than for smoking 2.56 (95% CI 1.9-3.5). Menezes et al added to these findings by reporting from Latin America, an increased risk of COPD by 4.1 times in men and 1.7 times in women with PPTB after adjustment for age, education, ethnicity, smoking, exposure to dust and smoke, childhood respiratory morbidity and comorbidities. Moreover, the findings suggested that the airflow limitation caused by TB was independent from smoking (18).

Similarly Lam et al (19) reported from China that, PPTB was independently associated with increased airflow obstruction (OR= 1.37, 95% CI, 1.13-1.67) even after adjusted for exposure to passive smoking, biomass fuel, and dust. The study also found that smoking did not modify the association between COPD and PPTB. In a recent study from Taiwan, Lee et al (20) also reported that apart from age, male sex and low income, a history of PTB is an independent risk factor for developing COPD [hazard ratio 2.05(1.768 -2.387)].

In the present study, the severity grades of COPD among PPTB subjects was 8.3% for mild, 58.3% for moderate, 16.7 % for both severe and very severe grades of obstruction according to the GOLD criteria (1). Noteworthy, in this study 8 (61.5%) out of the 13 subjects diagnosed

with lung function impairment had a combined obstructive-restrictive pattern, a finding consistent with former studies that suggested a mixed obstruction-restriction outcome as the most likely after TB (21). In the same manner, in a previous study of active PTB, Plit et al (52) found that FVC improved to a greater degree than FEV1 over the course of treatment. However in an another study including a small number of hospital based PPTB subjects, an obstructive pattern was more common than a mixed pattern (57).

In the present study, all the spirometric indicators before and after bronchodilator showed that, those with PPTB performed less well than the controls. PPTB was significantly associated with reduction in post-bronchodilator FEV1 values ($P<.001$), FVC values ($P<.001$) and FEV1/FVC ratio ($P=.009$). Menezes et al (18) reported similar findings, relying on post-bronchodilator spirometry. The same findings were also described previously in studies not based on the use of post-bronchodilator spirometry (25, 58).

The rationale for using post-bronchodilator test for diagnosing COPD is that subjects diagnosed with airflow obstruction may be asthmatic, hence GOLD (1) recommends the use of bronchodilator for the diagnosis of COPD. An asthma diagnosis is markedly less likely when a bronchodilator is used.

Out of the 13 subjects diagnosed with COPD in our study, there was only one subject who had actually a confirmed physician's diagnosis of COPD before inclusion in our study. This indicated that a substantial number of COPD patients could go undiagnosed in the community and further highlights the possibility of a high rate of under-diagnosis.

In this study, age was an independent risk factor for COPD, Subjects who were 60 years or more were at higher risk of COPD than subjects who were less than 40 years of age [OR=7.23 (95 % CI 1.58, 33.01)]. Old age is a known risk factor for COPD as mentioned earlier in several studies (20, 53, 55), the result from this study further supported this observation. However it is unclear whether healthy aging could lead to the development of COPD or that

age was reflecting on the cumulative exposure throughout life (1). It is important to state here that PPTB was an independent risk factor for COPD even after adjustment for age.

Although men are considered to have higher risk of COPD (1, 20, 53, 55), in the present study male sex did not imply an increased risk for COPD and there was not a significant association between gender and COPD. It is suggested that the increased risk of COPD among men is due to the higher prevalence of smoking and occupational exposures among men compared to women. However recent estimates from the high income countries showed that the prevalence of the disease is almost equal (1). Women are supposed to be at increased risk of COPD in low income countries because of exposure to smoke from biomass fuel (16). In this study, gender was not associated with COPD may be because of insignificant associations between smoking, occupational exposure to dust and smoke from biomass and COPD.

In this study, COPD was more prevalent in ever-smokers (6.2%) compared to non-smoker (4.3%), although the association was not significant ($P=0.55$). The increased prevalence in non-smokers observed in this study suggests that risk factors other than smoking could be involved. Smoking is considered as an important risk factor for COPD (1, 53-55). However, in this study smoking was not significantly associated with COPD and did not alter the association between PPTB and the risk of COPD. In fact, smoking was significantly associated with a reduction of FEV1/FVC ratio ($p=0.01$), but surprisingly, this association lost statistical significance when the ratio was converted to a categorical variable using the cutoff point < 0.7 (GOLD criteria). Two possible reasons could explain the lack of significant association between smoking and COPD. Firstly the strong association between PPTB and COPD seen in this study and secondly that the numbers of smokers was too small to give a significant association. Earlier Lam and his colleagues (19) noticed that smoking did not modify the association between PPTB and COPD, however, some (18) hypothesized that smoking and biomass smoke inhalation may actually compound the airflow obstruction caused by PTB.

Although several studies had established a higher risk of COPD with occupational exposure

(53, 54, 56), exposure to smoke from biomass fuel (16, 53-55), chronic comorbidities (16, 20), and BMI (54). In our study, none of these risk factors were associated with increased risk of COPD. That is most likely due to the low number of observations in this study in regards to the risk factors mentioned above.

Another important finding in this study was that, 20% of PPTB subjects who had delayed TB diagnosis and treatment, actually had airflow obstruction. This association between the delay in TB treatment and airflow obstruction was statistically significant ($P=.014$). Delayed TB treatment was an independent risk factor for COPD. In this respect, PPTB subjects who had delayed TB treatment were at 4.09 times higher risk than those who received treatment early [OR: 4.09 (95% CI 1.17-14.32)]. One particular finding from the study conducted by Lee et al (20) is of importance for the current study. They also found that delay in anti-TB treatment was an independent risk factor for COPD [hazard ratio 1.005 (1.003–1.007)]. In our study delayed TB treatment had higher odds for the risk of developing COPD. Lee et al (20) also indicated that the delay in TB treatment showed a dose-response relationship with the risk of developing COPD. Additionally the impact of TB remained for 6 years after TB diagnosis and was significant in females and older people (20). It is known that delay in TB diagnosis and treatment may result in more severe and aggressive forms of the disease. This could be a possible explanation for the association between delayed TB diagnosis and treatment and the risk of COPD. As reported from South Africa, Hnizdo et al (26) noticed that the severity of lung damage resulting in reduced pulmonary impairment was directly associated with the number of TB episodes among patients suffering from silicosis. That delayed TB diagnosis and treatment may result in lung damage the same manner as by multiple episodes of TB is also a possible explanation.

7.1 Limitations of the study

We were able to control some major confounding variables related to the risk factors of COPD by relying on post-bronchodilator spirometry and using fixed diagnostic criteria. By using the TB registers to ascertain PTB diagnosis, which is there based on sputum smear results also PTB is a quality assured diagnosis. The age and sex matching between the PPTB subjects and controls proved very good and allowed for comparison. Still, the study may have a number of potential limitations.

1. A cross-sectional design, although was suitable to estimate prevalence and to measure associations between exposures and outcomes, it is unable to show the direction of the association, that is to say whether PPTB occurred before COPD or vice versa. However, in this study we could argue that PPTB occurred first since the participants were included in the study after five years from having PTB and generally COPD occurs after the age of 40 years.
2. Patients with PPTB might over-report chronic respiratory symptoms. However, this is probably controlled by assessing their lung function and establishing the diagnosis of COPD by spirometry.
3. Participants with chronic respiratory conditions may be more likely to recall events like the delay in diagnosis and treatment of TB than those without such symptoms. This may have inflated the association between COPD and delayed treatment TB. But an OR of about 4 makes it unlikely that this association is only due to recall bias.
4. PPTB subjects were selected from the TB registers based on the existence of a cell phone contact number, thus some patients without cell phone might have been missed out. The use of cell phones was less common five years ago than nowadays in Sudan. This could have caused a selection bias. It is most likely that the study missed out some of the poorer patients. Also, patients dead or lost to follow up may have caused a

selection bias. Another issue in regards to selecting convenient sample is limitation in generalization.

5. The current sample size was convenient for the period of the study. But the total number of COPD subjects who were diagnosed was small. That was reflected in the wide confidence intervals, redundant variables and it made some associations difficult to establish.

8. CONCLUSION

The present study has identified that PPTB is significantly associated with COPD, and the prevalence of COPD among PPTB Sudanese adult subjects was 8.8%. Moreover PPTB was an independent risk factor and the strongest predictor for COPD with an odds ratio of 12.39 after adjusting for the major confounding risk factors such as age, gender, smoking, occupational exposure and exposure to smoke from biomass fuel. Furthermore, combined obstructive-restrictive lung function impairment was the most common pattern. However an obstructive alone pattern was also observed in four patients. As only one out of the 13 subjects diagnosed with COPD had a physician's diagnosis beforehand, under-diagnosis of COPD is probably common in Sudan especially among PPTB subjects. This study supplements the growing evidence of a strong association between PPTB and the risk of COPD.

Age was also a risk factor for COPD; participants who are at least 60 years of age had a higher risk of COPD compared to those who are under 40 years of age.

Smoking was not significantly associated with COPD and did not alter or modify the association between PPTB and COPD, although it was significantly associated with reduced FEV1/FVC ratio in post-bronchodilator spirometry.

Other risk factors such as occupational exposure, exposure to smoke from biomass fuel, chronic comorbidities and BMI were not significantly associated with COPD.

Another important finding in the study was that delayed TB treatment was an independent risk factor for COPD and the risk increased by 4.09 times in those who had delayed treatment compared to those had not.

8.1 Recommendations

We have identified important shortcomings and we would like to make the following recommendations

1. Set out a strategy for services for COPD similarly as the one in TB “how to identify these people and overcome current levels of late diagnosis” otherwise we should expect that physicians will be informed about the risk of developing COPD in patients with PPTB even if they are non-smokers.
2. Ensure early diagnosis and prompt initiation of PTB treatment and further follow up of PPTB patients, if the burden of COPD is to be reduced especially in countries with a high TB burden.
3. Estimate COPD prevalence, morbidity and mortality data and hopefully evaluate the social and economic burden related to COPD in Sudan.
4. Follow up studies with larger sample size would be useful to get a better picture of the impact of smoking and other risk factors and COPD.

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APPENDIX 1: QUESTIONNAIRE

Questionnaire: Prevalence and risk factors of COPD in past pulmonary tuberculosis patients in Khartoum State, Sudan

Name _____

Serial Number: ____

Age____/____/19____

Personal Data

Gender:

1. Female ()

2. Male ()

Marital Status

1.Single ()

2.Married ()

3. Divorced ()

4. Widowed ()

Address: _____

Ethnic group: _____

Education:

1. Illiterate ()

2. Non-formal ()

3. Primary ()

4. Secondary ()

5. University and above ()

Occupation

1. Unemployed ()

2. Retired ()

3. Worker ()

4. Employed ()

5. Freelancer ()

6. Others (), specify: _____

Monthly Salary:

1. < 500 SDG ()

2. 500-1000 SDG ()

3. 1001-2000 SDG ()

4. >2000 SDG ()

Type

1. Past pulmonary TB case ()

2. Control ()

If a past pulmonary TB case

After the symptoms started have you been diagnosed and started treatment directly

1. Yes ()

2. No ()

If No

1. Why: _____

2. For how long till you started treatment? _____month

Respiratory symptoms

Cough

1. Do you usually have cough that is not associated with cold?

1. Yes ()

2. No ()

If yes,

2. Do you cough most of the days for 3 consecutive months or more during a year?

1. Yes ()

2. No ()

3. If yes, for how many years do you have this cough?

1. Less than 2 years ()

2. 2-5 years ()

3. More than 5 years ()

1. Do you usually bring up phlegm from your chest?

- ## Wheeze

- ## Shortness of breath

- ### Past illness

- 64

1. Yes () 2. No ()

1. Yes () 2. No ()

1. Yes () 2. No ()

1. Yes () 2. No ()

6. Have you ever had heart disease?

6.1 If yes, was it confirmed by doctor?

1. Yes () 2. No ()

1.1 Have you ever smoked cigarettes?

1. Yes () 2. No ()

1.2 How old were you when started smoking? _____ Years

1.3 Do you still smoke?

1. Yes () 2. No ()

1.4 How many cigarettes do you smoke per day? _____ Cigarettes

1.5 On the average of the entire time you smoked how many cigarettes did you smoke per day? _____Cigarettes

2.1 Have you ever smoked water pipe?

1. Yes () 2. No ()

2.2 How old were you when started smoking? _____ Years

2.3 Do you still smoke?

1. Yes () 2. No ()

2.4 How many shisha do you smoke per day? _____ shisha

3.1 Did you ever live with someone who smokes?

1. Yes () 2. No ()

1. Do you have a family history of chronic lung conditions?

1. Yes () 2. No ()

2. If yes, please specify? _____

1. Do you have any other chronic illness?

1. Yes () 2. No ()

If yes, please specify? _____

1. Have you ever worked for a year or more in any dusty job?

1. Yes () 2. No ()

1.2 If yes, please specify? _____

1.3 Dust exposure:

1. Mild () 2. Moderate () 3. Severe ()

2. Have you ever been exposed to gas or chemical fumes at work?

1. Yes () 2. No ()

2.2 If yes, please specify? _____

2.3 Fumes exposure:

1. Mild () 2. Moderate () 3. Severe ()

Biomass smoke exposure

1. Do you use biomass fuel for heating or cooking?

1. Yes () 2. No ()

APPENDIX 2: INFORMED CONSENT

PART 1: Information Sheet

You are invited to participate in a study about the prevalence and risk factors of COPD in past pulmonary tuberculosis patients. It is very important that you read and understand the following information. The information given is to describe the purpose, procedures, benefits and risks of the research study. There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask me about them. You do not need to decide today whether or not you will participate in the study. Before you take your decision, you can talk to anyone you feel comfortable with about this study. You may refuse to take part or withdraw from this study at any time.

Introduction

This study is aimed to measure Chronic Obstructive Pulmonary Disease (COPD) in past tuberculosis patients and healthy controls.

COPD stands for chronic obstructive pulmonary disease

Chronic means it will not go away

Obstructive means partly blocked

Pulmonary means in the lungs

Disease means illness

COPD obstructs the airways and results in breathing difficulties. Risk factors for COPD include smoking, exposure to fumes and dust at work, biomass smoke exposure and past pulmonary tuberculosis. COPD cannot be cured however it can be treated. The earlier it is detected the better the results of treatment.

COPD is the third leading cause of death worldwide; our current knowledge about COPD in our community is not complete.

Purpose of the study

The purpose of this study is to measure the prevalence and associated risk factors of COPD in people with past history of pulmonary tuberculosis compared to people without history of pulmonary tuberculosis

Participants

We are inviting all adults (Men and Women) aiming to include a total of 270 participants. People included in this study are either

1. Healthy people
2. People with past history of pulmonary tuberculosis

Study protocol and procedures

The study procedures and protocol will be carefully explained to you, and if you need more information you can freely ask about them whenever you would like. No procedure will be initiated before you offer your consent to participate in the study.

1. Questionnaire

You will be asked questions about your medical history such as presence of respiratory symptoms (cough, phlegm, wheezing, shortness of breath), exposure to potential risk factors, respiratory diseases (asthma, COPD, chronic bronchitis, etc.) and other diseases. The questionnaire will take approximately 30 minutes to be completed.

2. Pulmonary Function Test (spirometry)

Your pulmonary function will be tested using a device called spirometry both before and after administration of inhaled bronchodilator drug, these are standard procedures for lung function testing. You will perform at least 3 breathing test before and after 15 minutes of inhaling 4 puffs of a bronchodilator called salbutamol (Ventolin) a standard drug used by asthmatic and COPD patients so as to relax the airways and relieve symptoms. In your case the use of this drug is part of the routine procedure for spirometry testing in all subjects as it allows us to measure your best lung function, when the airways are fully relaxed.

Potential risks and discomfort

1. Questionnaires: You do not have to answer any question that you do not feel comfortable with. Any information that you provide to the researcher is completely confidential and you will not be identified.

2. Symptoms: Before the test, you will be asked to withhold some of your respiratory medication (if you have any). However if you feel you need to use your medications, you should use them as you would normally do. The researcher will explain how many hours before the test you should withhold your respiratory medications. You will be able to take them once the test is completed. As a result of withholding the medicines you could feel more shortness of breath. This is temporary and could be quickly relieved by using your usual bronchodilator if it becomes too serious. Please tell the researcher if you were unable to withhold your respiratory medicines.

3. Spirometry: It is unusual to have discomfort, however some people may experience headache, and or dizziness when performing the test, these feeling are generally temporal. This test is the standard test for lung function and is performed in patients and normal subjects worldwide. Spirometry is not dangerous and does not involve any painful procedures such as needles. However you have to breathe out with maximal effort and thus you may feel dizzy or lightheaded. So to reduce the risk of this, the breathing test is performed as you are seated in a chair. The researcher was specially trained and certified in this procedure.

Potential benefits

There are no direct benefits to you from participating in this study. The indirect benefit associated with participation in the study include

1. You may have undiagnosed COPD, which may be identified in this study. If so you will be encouraged to see a chest physician for treatment.
2. You will know your lung function status which, like knowing your blood pressure or blood sugar, which is of value to your health.
3. You may have the satisfaction of participating in an important study of lung health with wide public health implications.

Benefits for the community

1. The prevalence of COPD in the community
2. The prevalence of COPD in the past pulmonary TB patients
3. The role of past pulmonary TB, smoking and non-smoking risk factors in the development of COPD

Confidentiality

Your confidentiality will be respected. No information that discloses your identity will be released or published. On papers, questionnaire, files and test for the study and any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except your physician upon your request.

Right to refuse or withdraw

You do not have to participate in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. This will not affect your relationship with the clinic staff or the researcher. Your choice and rights will still be respected

Who to Contact

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact

Dr. Rashid Osman

Telephone: 012927665

PART 2: Informed Consent Certificate

I have read the above information, or it has been read to me. And I have had the chance to ask questions. Any questions that I have asked have been answered clearly with pleasure.

I consent voluntarily to participate as a participant in this research.

Name of participant _____ Date _____

Signature of participant _____

Name of witness _____ Date _____

Signature of witness _____

Name of researcher _____ Date _____

Signature of researcher _____

- YOU WILL BE GIVEN A COPY OF THIS FORM

APPENDIX 3: ARABIC QUESTIONNAIRE

استبيان عن عوامل انتشار و الخطورة لمرض الرئة الانسدادي المزمن لمرضى السل الرئوي السابق في ولايه

الخرطوم-السودان:

الرقم التسلسلي : ____

البيانات الشخصية

الاسم: _____

العمر: 19 / /

الجنس: 1. أنثى ()

الحالة الاجتماعية 1. أعزب ()

العنوان: _____

القبيلة: _____

التعليم: _____

1. أمي ()

2. غير النظامي/خلوة ()

3. الابتدائي/ اساس ()

4. الثانوي ()

5. جامعي أو ما فوق ()

المهنة: _____

1. عاطل ()

2. معاشي ()

3. عامل ()

4. موظف ()

5. اعمال حرة ()

6. اخري ()

الراتب الشهري: _____

1. أقل من 500 ج ()

2. 500 - 1000 ج ()

3. 1001 - 2000 ج ()

2. أكثر من 2000 ج ()

نوع الحالة

1. سل رئوي سابق ()

إذا كانت حالة سل رئوي سابق،

بعد بداية الاعراض هل تم شخيصك و بدأت العلاج مباشرة؟

1. نعم ()

2. لا ()

إذا كانت الإجابة بلا ،

1. لماذا؟ _____

2. بعد كم من الزمن بدأت العلاج؟ شهر _____

أعراض الجهاز التنفسي

سعال

1. هل لديك عادة سعال لا يرتبط مع البرد ؟

1. نعم ()

2. لا ()

إذا كانت الإجابة بنعم ،

2. هل السعال في معظم الأيام لمدة 3 أشهر متتالية أو أكثر خلال السنة؟

1. نعم ()

2. لا ()

3. إذا كان الجواب نعم ، كم سنة لديك هذا السعال ؟

1. أقل من 2 سنة ()

2. 2-5 سنوات ()

3. أكثر من 5 سنوات ()

بلغم

1. هل عادة تخرج بلغم من صدرك ؟
 1. نعم ()
 2. لا ()
2. هل عادة تخرج البلغم في معظم الأيام لمدة 3 أشهر متتالية أو أكثر خلال السنة؟
 1. نعم ()
 2. لا ()
3. إذا كان الجواب نعم ، كم سنة لديك هذا البلغم ؟
 1. أقل من 2 سنة ()
 2. 2-5 سنوات ()
 3. أكثر من 5 سنوات ()

أزيز أو صفير الصدر

1. هل لديك أزيز أو صوت صفير في الصدر في السنة الماضية؟
 1. نعم ()
 2. لا ()
2. إذا كانت الإجابة بنعم ، هل كان لديك هذا الأزيز ولم يكن لديك برد ؟
 1. نعم ()
 2. لا ()
3. هل شعرت بضيق في التنفس عندما يكون لديك هذا الأزيز ؟
 1. نعم ()
 2. لا ()
4. كم سنة لديك هذا الأزيز ؟
 1. أقل من 2 سنة ()
 2. 2-5 سنوات ()
 3. أكثر من 5 سنوات ()
5. هل حدث لك في أي وقت مضى نوبة أزيز و ضيق في التنفس ؟
 1. نعم ()
 2. لا ()
6. كم كان عمرك عندما حدثت لك أول نوبة ؟ _____ سنوات

ضيق التنفس

1. هل حدث لك ضيق في التنفس بدون بذل جهد خلال السنة الماضية؟
 1. نعم ()
 2. لا ()
2. هل حدث لك ضيق في التنفس بعد ان بذلت جهداً خلال السنة الماضية؟
 1. نعم ()
 2. لا ()
3. هل حدث أن استيقظت بضيق في التنفس خلال الثلاثة شهور الماضية ؟
 1. نعم ()
 2. لا ()
4. إذا كان الجواب نعم ، كم مرة في الأسبوع استيقظت بضيق في التنفس خلال الثلاثة شهور الماضية ؟ _____ مرة
5. هل تشعر بضيق في التنفس عند الاسراع أو خلال صعود مكان عالي نسبياً؟
 1. نعم ()
 2. لا ()
6. هل تضطر الي المشي بصورة أبطأ من الناس الذين في عمرك بسبب ضيق في التنفس ؟
 1. نعم ()
 2. لا ()
7. هل تضطر الي التوقف للتنفس عند المشي اذا كنت تسير على مستوى غير عالي؟
 1. نعم ()
 2. لا ()
8. هل تشعر بضيق التنفس لمغادرة المنزل أو عند لبس أو خلع ملابسك ؟
 1. نعم ()
 2. لا ()

الامراض السابقة

1. هل لديك أي مشكلة في الرئة قبل سن الـ 16 ؟
 1. نعم ()
 2. لا ()
2. هل كان لديك في أي وقت مضى مرض الربو الشعبي\الازما ؟
 1. نعم ()
 2. لا ()
2. إذا كانت الإجابة بنعم ، هل تم تاييده بواسطه الطبيب ؟
 1. نعم ()
 2. لا ()
- 3.2 كم كان عمرك عندما حدثت لك أول نوبة للربو الشعبي ؟ _____ سنوات
- 4.2 إذا لم يعد لديك ربو ، في أي عمر توقف؟ _____ سنوات
3. هل كان لديك في أي وقت مضى مرض التهاب الشعب الهوائية المزمن ؟
 1. نعم ()
 2. لا ()
- 1.3 إذا كان الجواب نعم ، هل تم تاييده بواسطه الطبيب ؟
 1. نعم ()
 2. لا ()
- 2.3 في أي عمر بدأ هذا المرض؟ _____ سنوات

4. هل كان لديك في أي وقت مضى مرض انتفاخ الرئة (انفسيم) ؟

1. نعم () 2. لا ()

1.4 إذا كان الجواب نعم ، هل تم تاييده بواسطة الطبيب ؟

1. نعم () 2. لا ()

2.4 في أي عمر بدأ هذا المرض؟ _____ سنوات

5. هل كان لديك في أي وقت مضى أي من امراض الصدر الأخرى؟

1. نعم () 2. لا ()

1.5 إذا كانت الإجابة بنعم يرجى التحديد ؟ _____

6. هل كان لديك في أي وقت مضى أمراض القلب ؟

1. نعم () 2. لا ()

1.6 إذا كان الجواب نعم ، هل تم تاييده بواسطة الطبيب ؟

1. نعم () 2. لا ()

التدخين

1. السجائر

1.1 هل سبق لك أن دخنت السجائر ؟ (أكثر من 20 علبة في العمر أو أكثر من سيجارة واحدة في اليوم لمدة عام)

1. نعم () 2. لا ()

إذا كانت الإجابة بنعم،

2.1 كم كان عمرك عندما بدأت تدخين السجائر بصفة منتظمة؟ _____ سنوات

3.1 هل ما زلت تدخن؟

1. نعم () 2. لا ()

4.1 كم سيجارة تدخن في اليوم ؟ _____

5.1 في المتوسط من الوقت الذي كنت فيه مدخن, كم سيجارة كنت تدخن يوميا؟ _____

2. الشيشة

1.2 هل سبق لك أن دخنت الشيشة ؟ (أكثر من حجر شيشة في الاسبوع لمدة سنة في أي فترة من فترات حياتك)

1. نعم () 2. لا ()

إذا كانت الإجابة بنعم،

2.2 كم كان عمرك عندما بدأت تدخين الشيشة بصفة منتظمة؟ _____ سنوات

3.2 هل ما زلت تدخن؟

1. نعم () 2. لا ()

4.2 كم حجر شيشة تدخن في اليوم أو الاسبوع ؟ _____

3. التدخين السالب

3. هل كنت تعيش في أي وقت مضى مع شخص يدخن ؟

1. نعم () 2. لا ()

التاريخ الأسري

1. هل لديك تاريخ عائلي لأمراض الصدر المزمنة ؟

1. نعم () 2. لا ()

2. إذا كانت الإجابة بنعم ، يرجى التحديد ؟ _____

التاريخ المرضي

1. هل لديك أي مرض مزمن آخر؟

1. نعم () 2. لا ()

2. إذا كانت الإجابة بنعم ، يرجى التحديد ؟ _____

التعرض المهني

1 . هل عملت في أي وقت مضى لمدة عام أو أكثر في أي وظيفة متربة ؟

1. نعم () 2. لا ()

2.1 إذا كانت الإجابة بنعم ، يرجى التحديد ؟ _____

3.1 التعرض للغبار :

1. خفيف () 2. معتدل () 3. شديد ()

2 . هل سبق لك أن تعرضت لغاز أو أبخرة كيميائية في العمل؟

1. نعم () 2. لا ()

2.2 إذا كانت الإجابة بنعم ، يرجى التحديد ؟ _____

3.2 التعرض للدخنة :

1. خفيف () 2. معتدل () 3. شديد ()

التعرض لدخان الوقود الصلب

1 . هل تستخدم الوقود الصلب (فحم/حطب) لأغراض التدفئة أو الطبخ ؟

1. نعم () 2. لا ()

APPENDIX 4: ARABIC QUESTIONNAIRE

الجزء الأول: ورقة معلومات

أنت مدعو للمشاركة في دراسة حول عوامل الانتشار والخطورة لمرض الرئة الانسدادي المزمن في مرضى السمل الرئوي السابقين. إنه من الأهمية أن تقرأ وتفهم المعلومات التالية. المعلومات المقدمة الهدف منها وصف الغرض والإجراءات والفوائد والمخاطر من هذه الدراسة البحثية. قد يكون هناك بعض الكلمات التي لا تفهمها. من فضلك اسألني للتوقف ونحن نمضي من خلال هذه المعلومات وقد يستغرق الشرح وقتا. إذا كانت لديك أسئلة في وقت لاحق، يمكنك أن تسألني، لا يجب عليك أن تقرر اليوم ما إذا كنت تود أن تشارك أو لا تشارك في البحث. قبل أن تقرر، يمكنك التحدث إلى أي شخص تشعر بالراحة معه عن البحث. يحق لك أن ترفض المشاركة أو الانسحاب من هذه الدراسة في أي وقت

مقدمة

تم تصميم هذه الدراسة لقياس مرض الانسداد الرئوي المزمن (COPD) في مرضى السمل السابقين والأشخاص الأصحاء

COPD ترمز لمرض الانسداد الرئوي المزمن

المزمن يعني أنه لن يزول نهائيا

الانسداد يعني سدد جزئيا

مرض الانسداد الرئوي المزمن يقوم بسد الشعب الهوائية مما يؤدي إلى صعوبات في التنفس. وتشمل عوامل الخطورة المسببة لمرض الانسداد الرئوي المزمن، التدخين، والتعرض للأبخرة وأماكن العمل المتربة، واستنشاق دخان الفحم والاصابة القديمة بمرض السمل الرئوي. لا يمكن الشفاء من هذا المرض ولكن يمكن التعامل معه. اذا تم كشف هذا المرض مبكرا ستكون نتائج العلاج أفضل غالبا. مرض الرئة الانسدادي المزمن هو ثالث سبب رئيسي للوفاة في العالم؛ ومعرفتنا الحالية حول هذا المرض في مجتمعنا ليست كاملة.

الغرض من البحث

الغرض من هذه الدراسة هو قياس معدل انتشار هذا المرض وعوامل الخطر المسببة او المرتبطة به في الأشخاص الذين تمت اصابتهم بمرض السمل الرئوي سابقا مقارنة بأشخاص أصحاء ليست لديهم أي اصابه بمرض السمل الرئوي سابقا

المشاركين جميع البالغين (رجال ونساء) بهدف أن تشمل ما مجموعه 270 مشاركا الأشخاص الذين تشملهم هذه الدراسة والمشاركين هم

1. أشخاص أصحاء

2. أشخاص مصابين سابقا بمرض السمل الرئوي

2. إجراءات وبروتوكول الدراسة

سيتم شرح إجراءات وبروتوكول الدراسة لك بعناية ، اذا كنت بحاجة الى مزيد من المعلومات يمكنك أن تسأل كلما كنت ترغب في ذلك .وسوف لن يتم القيام بأي إجراء قبل أن توافق على المشاركة في الدراسة

1. الاستبيان

سوف يتم سؤالك اسئلة تتعلق بتاريخك المرضي مثل وجود أعراض تنفسية (سعال ، بلغم، أزيز، وضيق التنفس)، التعرض لعوامل الخطر المحتملة، أمراض الجهاز التنفسي (الربو، مرض الانسداد الرئوي المزمن، التهاب الشعب الهوائية المزمن، الخ) وغيرها من الأمراض.

الاستبيان قد يستغرق حوالي 30 دقيقة لإكماله

2. اختبار وظيفة الرئة (قياس التنفس)

سوف تخضع لاختبار وظائف الرئة بواسطة جهاز (قياس التنفس) قبل وبعد اخذك جرعة من بخاخ موسع الشعب الهوائية، تلك هي الإجراءات القياسية لاختبار وظيفة الرئة .سوف يتم إجراء اختبار التنفس علي الأقل 3 مرات قبل وبعد 15 دقيقة من استنشاقك 4 بخات من موسع الشعب الهوائية بخاخ سالبوتامول (فينتولين) وهو الدواء المستخدم من قبل مرضى الربو ومرضى الانسداد الرئوي المزمن لاسترخاء الشعب الهوائية وتخفيف الأعراض .

استخدام هذا الدواء هو جزء من الإجراءات الروتينية لاختبار قياس التنفس لجميع الناس لأنها تسمح لنا بقياس أفضل وظيفة رئة لديك ، عندما تكون الشعب الهوائية مسترخية تماما .

المخاطر المحتملة والازعاجات

1.الاستبيان: لا يجب عليك الرد على أي سؤال أن كنت لا تشعر بالراحة له .كل ما تقوله للباحث سيكون سري تماما، وهذا يعني انه لن يتم معرفتك.

2.الأعراض: قبل الاختبار سوف يطلب منك الامتناع عن اخذ بعض الأدوية التنفسية الخاص بك (إذا كان لديك) . ولكن إذا كنت تشعر بأنك بحاجة إلى استخدام الأدوية الخاصة بك، يجب عليك استخدامها كما تفعل عادة . الباحث سوف يخبرك قبل كم ساعة من الاختبار يجب عليك الامتناع عن ادوية الجهاز التنفسي الخاصة بك .وسوف يمكنك اخذها بمجرد الانتهاء من الاختبار .نتيجة للامتناع عن اخذ الأدوية قد تشعر بضيق في التنفس .سوف يكون هذا مؤقتا ويمكن أن يزول وبسرعة باستخدامك لبخاخك المعتاد. يرجى إبلاغ الباحث إذا كنت غير قادر عن الامتناع من اخذ أدويةك التنفسية.

3. اختبار قياس التنفس: من غير المعتاد ان تحدث لك أنزعاجات جراء أداءك اختبار قياس التنفس ، لكن بعض الناس قد يعانون من الصداع، أو الدوخة عند الاختبار، وعادة ما تكون هذه الانزعاجات مؤقتة . اختبار قياس التنفس هو الاختبار القياسي لوظائف الرئة، ويتم إجراء هذا الاختبار علي المرضى والاصحاء في جميع أنحاء العالم .قياس التنفس آمن ولا يشمل اي إبر .ولكن الاختبار يتطلب على أقصى جهد من الزفير، وهذا قد يشعرك بالصداع أو بالدوار .للحد من هذه المخاطر ، يتم تنفيذ اختبار التنفس وأنت جالس على كرسي .تم تدريب الباحث خصيصا للقيام بهذا الاختبار ولديه شهادته لإجراء الاختبار.

الفوائد المحتملة

- لا توجد فوائد مباشرة لصالحك من المشاركة في هذه الدراسة
- الفوائد الغير المباشرة لصالحك والمرتبطة بالمشاركة في الدراسة هي ما يلي
1. قد يكون لديك هذا المرض ولم يتم تشخيصك من قبل ، الذي قد يتم الكشف عنه في هذه الدراسة .إذا كان الأمر كذلك سوف يتم تشجيعك لأن تقابل الطبيب لتلقي العلاج.
 2. سوف تعرف الحالة الراهنة لوظيفة رئتك والتي، هي مثل معرفة ضغط الدم أو نسبة السكر في الدم لديك، وهذا من المهم لصحتك.
 3. قد تشعر بالرضا من المشاركة في دراسة هامة لصحة الرئة وذات فوائد جمة للصحة العامة.

الفوائد التي تعود على المجتمع

1. قياس معدل انتشار مرض الانسداد الرئوي المزمن في المجتمع
2. قياس معدل انتشار مرض الانسداد الرئوي المزمن في مرضى السل الرئوي السابق
3. دور السل الرئوي السابق والتدخين وعوامل الخطورة الغير متعلقة بالتدخين في خطر الإصابة بمرض الانسداد الرئوي المزمن

الخصوصية

سيتم احترام سريتك تماما. لن يتم البوح أو نشر أي معلومات تكشف عن هويتك .سيتم وضع رقم بدلا من اسمك على أي أوراق، أو استبيان، أو ملفات أو اختبار ووظائف الرئة أو أي معلومات عنك .فقط الباحث يمكنه معرفة ما هو رقمك وسوف يتم قفل تلك المعلومات .لن يتم الإفصاح أو تعطى أي معلومة لأحد إلا للطبيب المعالج بناء على طلبك.

الحق في رفض المشاركة أو الانسحاب من البحث

لا يستوجب عليك المشاركة في هذا البحث إذا كنت لا ترغب في القيام بذلك .تستطيع أيضا الانسحاب من المشاركة في البحث في أي وقت تختاره .هذا لن يؤثر على علاقتك مع الطبيب المسؤول عن العيادة أو الباحث .هذا اختيارك وجميع حقوقك ستحترم

بمن تتصل

إذا كان لديك أي أسئلة يمكنك أن تسأل الآن أو في أي وقت لاحق، أو حتى بعد بدء الدراسة .إذا كنت ترغب في طرح الأسئلة في وقت لاحق، يمكنك الاتصال

الدكتور راشد عثمان

الهاتف: 012927665

الجزء الثاني: شهادة الموافقة

لقد قرأت المعلومات السابقة، أو تم قراءتها لي

وقد أتيت لي الفرصة لطرح الأسئلة حول هذا الموضوع ولقد تمت الإجابة على أي أسئلة طرحتها بارتياح

أوافق طوعا للمشاركة كمشارك في هذا البحث

اسم المشارك _____ التاريخ _____

توقيع المشارك _____

اسم الشاهد _____ التاريخ _____

توقيع الشاهد _____

اسم الباحث _____ التاريخ _____

توقيع الباحث _____

- سوف تعطى صورة من هذا النموذج

APPENDIX 5: NORWAY (REK) ETHICAL CLEARANCE CERTIFICATE



Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Katrine Ore	22845517	03.07.2013	2013/1085/REK sør-øst A
			Deres dato:	Deres referanse:
			28.05.2013	
Vår referanse må oppgis ved alle henvendelser				

Gunnar Aksel Bjune
postboks 1130 Blindern

2013/1085 Prevalence and risk factors of COPD in past pulmonary TB patients, in Khartoum State, Sudan

Institution responsible for the research: Department of community health, Epilab
Project Manager: Gunnar Aksel Bjune

The Committee reviewed the application during its meeting on the 20th of June 2013. The project was assessed in accordance with the Norwegian Research Ethics Act of 2006 and ACT 2008-06-20 no. 44: Act on medical and health research (the Health Research Act)

The Project

The Committee reviewed the application during its meeting on the 20th of June 2013. The project was assessed in accordance with the Norwegian Research Ethics Act of 2006 and ACT 2008-06-20 no. 44: Act on medical and health research (the Health Research Act) The project Chronic obstructive pulmonary disease (COPD) and pulmonary tuberculosis (PTB) are significant health problems especially in low and middle income countries. Although smoking is recognized as the main risk factor for COPD, there is an increasing interest in non-tobacco risk factors. There is growing evidence that PTB is a risk factor for COPD.

The aim of this study is to estimate the prevalence and the risk factors of COPD among past pulmonary TB patients.

The study aims to provide data about the prevalence and risk factors of COPD among past PTB patients, add to the existing knowledge about COPD and PTB sequel in one of the low income countries.

Aiming to measure the prevalence and risk factors of COPD among past pulmonary TB patients, retrospective cohort will be conducted in Khartoum, Sudan.

A total of 135 Past PTB subjects will be selected randomly from TB registers matched to a control group.

Structured questionnaires will be used during face to face interview for collecting data after meeting the inclusion criteria.

COPD will be established using symptoms and lung function tests using spirometry.

The Committee's evaluation of the project

The committee find the study well designed. We will recommend the following amendments for the Participant Information Sheet:

Besøksadresse:
Gullhaugveien 1-3, 0484 Oslo

Telefon: 22845511
E-post: post@helseforskning.etikkom.no
Web: <http://helseforskning.etikkom.no/>

All post og e-post som inngår i
saksbehandlingen, bes adressert til REK
sør-øst og ikke til enkelte personer

Kindly address all mail and e-mails to
the Regional Ethics Committee, REK
sør-øst, not to individual staff

TB should be written tuberculosis (TB) when first mentioned in the Information Sheet

The following sentence: "This is a request for you to participate in a research study." needs to be amended:
"This is an inquiry for you to participate in a research study"

The Committee presume that the information sheet will be available in the local languages.

Committee's decision

The Committee has reviewed the application and approved it in accordance with the Health Research Act paragraph 9.

The approval is based on the grounds that the project is implemented as described in the application and the protocol, as well as the guidelines stated in the Health Research Act.

If amendments need to be made to the study, the Chief Investigator is required to submit these amendments for approval by REC via the amendment form. Please note that if the amendments are considered to be substantial to the project, REC may request that a new project application is sent.

The personal health data collected for the project is to be stored according to standard regulations.

The project is approved until 31.12.2013.

Med vennlig hilsen

Gunnar Nicolaysen
Professor
Leder

Katrine Ore
Rådgiver

Kopi til: g.a.bjune@medisin.uio.no; r.k.k.osman@studmed.uio.no

APPENDIX 6: SUDAN ETHICAL CLEARANCE CERTIFICATE

Republic of Sudan
National Ministry of Health

HEALTH RESEARCH COUNCIL

NATIONAL RESEARCH ETHICS REVIEW COMMITTEE

Date: 5/12/2013

Provisional Ethical Clearance Certificate

This is to certify that the proposal entitled (Prevalence and factors of COPD in past Pulmonary patients , in Khartoum State, Sudan) submitted by: Dr. Rashid Kamal Khalid Osman , from University of Oslo, has been approved by the National Health Research Ethics Committee, Federal Ministry of Health to be carried out in the Sudan.

NB

The final ethics clearance certificate will be granted after submission of the final report to the Research Directorate- Federal Ministry of Health.

5/6/2013
Dr. Iwan Abdalla Mustafa
Reporter of the
National Research Ethics Review Committee

